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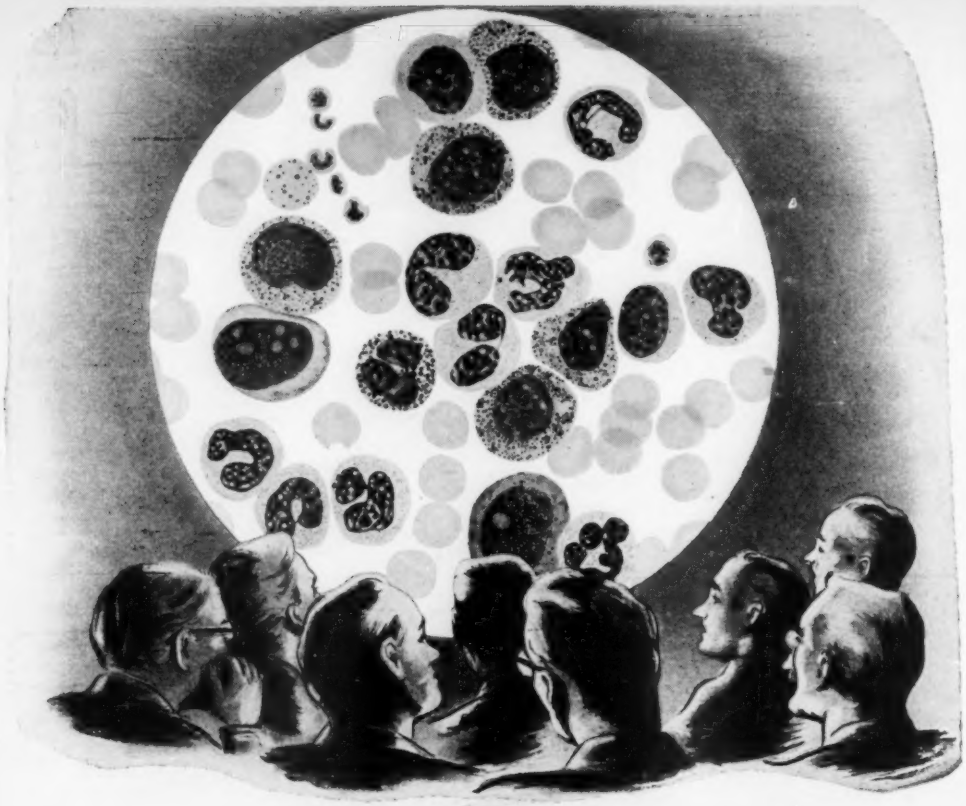

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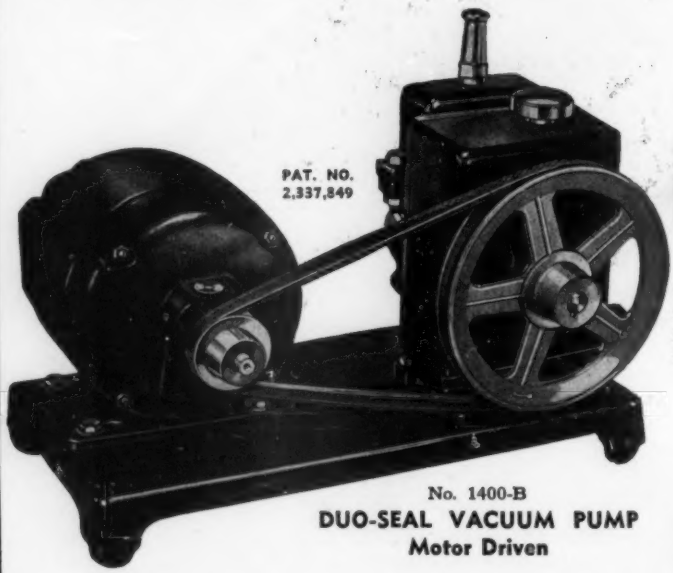

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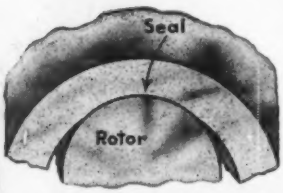

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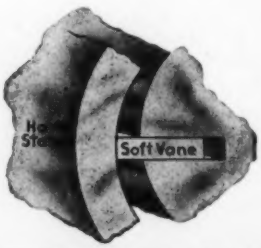

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Trace Minerals in Food Production and Health

SCIENTISTS face no greater problem than that of assuring that the earth's rising population be adequately clothed, housed, and fed. Such assurance is essential if permanent world peace is to be attained. Achievement of this objective demands effort on many fronts: improved agricultural science, chemurgy, greater utilization of photosynthetic energy, novel foods and construction materials, the harnessing of microlife, and exploitation of marine resources. Among the possibilities is the increase of agricultural production and the nutritive value of foods by furnishing to deficient soils the minerals essential to high productivity and to the food quality upon which human health depends.

In addition to the major nutrients—nitrogen, phosphorus, and potassium—plants require small amounts of "trace minerals" such as copper, zinc, iron, manganese, and molybdenum. The animal body has similar requirements, since the trace minerals, among their other vital functions, are indispensable to the enzymatic control of plant and animal physiology.

Severe deficiencies of trace minerals in the soil and diet produce a wide range of striking pathological conditions in plants, livestock, and man. More dangerous are the often unrecognized subclinical deficiencies, which prevent crops from attaining full productive potentialities, subtly restrain the growth of animals, and depress the general level of human health without inducing well-defined disease.

Trace-mineral deficiencies in soil, reflected in lowered essential mineral content of foods, are worldwide. Recent experience, especially in the United States, Great Britain, Australia, and New Zealand, has shown the important increases in crop production that are attainable by supplying small amounts of the trace minerals to soils that may not have been suspected of deficiency. There can be little doubt of the added benefit to human health.

The growing interest in trace minerals in plant and animal nutrition is seen in the growing number of programs on trace-mineral research at The Johns Hopkins University; MIT; Battelle Institute; the agricultural experiment stations of New Jersey, Missouri, Florida, Wisconsin, and California; the U. S. Soil, Plant, and Nutrition Laboratory; Rowett and Macaulay Institutes in Scotland; and others.

Although much remains to be learned of the fundamentals and applications of trace-mineral nutrition, the growing practical achievements of trace-mineral therapy have opened the way for widespread improvement in agricultural production and human health.

A bottleneck to research and practice in this field is the expensive equipment, skills, and resulting high cost of trace-mineral analyses of soils, crops, and foods, and of animal and human samples. This bottleneck could be broken by provision of a central analytical laboratory where the methods of the industrial production line could be used in complete and highly accurate analyses of hundreds of thousands of samples annually. The basic instrument would be the electronic recording spectrograph (quantometer), which has a theoretical capacity of a million samples of quantitative trace-mineral analyses per year, serving researchers, agriculturists, nutritionists, and medicine, internationally.

The laboratory would not interpret individual analyses; rather, it should supply new, needed data to aid diagnosis and treatment by specialists and practitioners in the fields served. The task of the laboratory we visualize extends beyond routine analyses. The data, if studied by competent investigators, would permit research by statistical methods, gradually clarifying the relationships between soil, agricultural production, and human health. In addition to revealing soil, food, and human deficiencies around the world, it would aid in the discovery of new mineral resources.

It can be predicted with confidence that the United States, as well as other countries, will some day have adequate analytical laboratories, and that their functioning will contribute notably to human well-being.

K. STARR CHESTER

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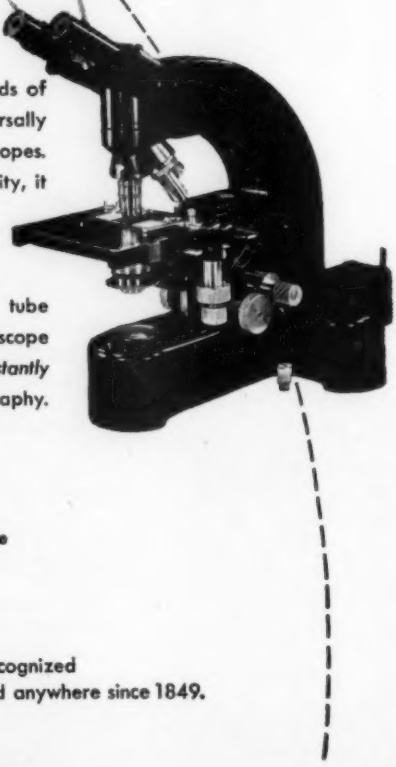

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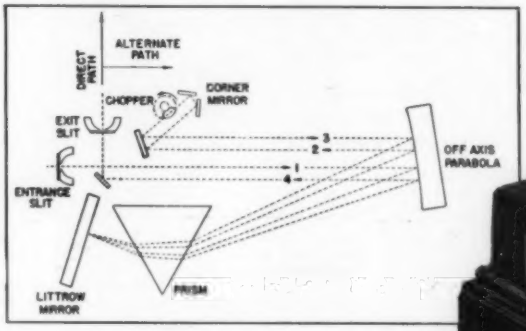

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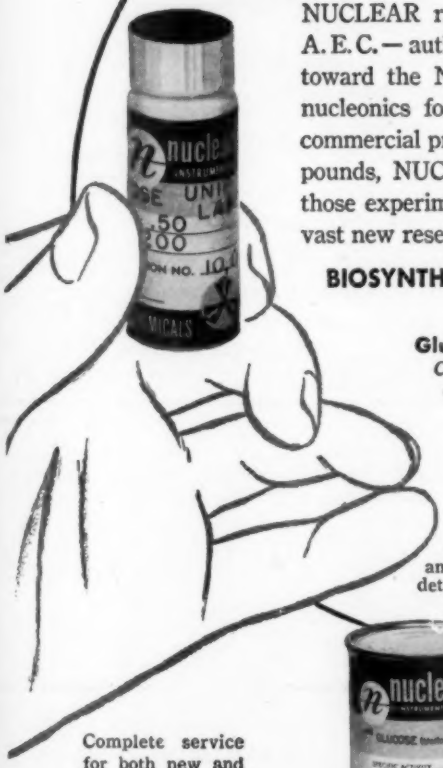

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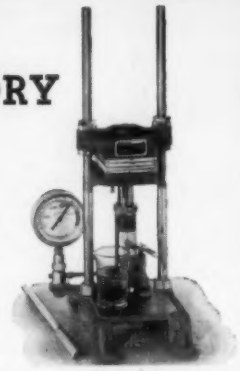

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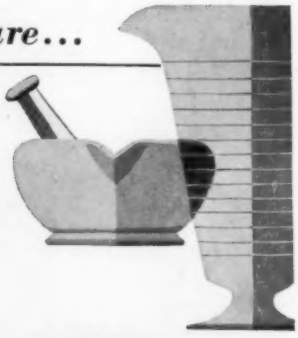

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"I can remember," *wrote G. H. Hardy,* "Bertrand Russell telling me of a horrible dream . . .

"HE was in the top floor of the University Library, about A.D. 2100. A library assistant was going round the shelves carrying an enormous bucket, taking down book after book, glancing at them, restoring them to the shelves or dumping them into the bucket. At last he came to three large volumes which Russell could recognize as the last surviving copy of PRINCIPIA MATHEMATICA. He took down one of the volumes, turned over a few pages, seemed puzzled for a moment by the curious symbolism, closed the volume, balanced it in his hand and hesitated . . ."

No one need doubt today what the librarian's decision would be in the year 2100. PRINCIPIA MATHEMATICA is an epoch-making work which started a new era in mathematical logic and the foundations of mathematics. Since the appearance of the first edition of 1910-1913, interest in mathematical logic has steadily increased. Controversies have been vigorous and exciting and have succeeded in clearing the mathematical air. But through it all PRINCIPIA MATHEMATICA has stood out as a landmark in the history of human thought.

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History and Development of Chemical Periodicals in the Field of Organic Chemistry: 1877–1949[1]

Fletcher S. Boig
Department of Chemistry, Northeastern University, Boston, Massachusetts
Paul W. Howerton
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CONSIDERABLE INTEREST has recently been shown by chemists in periodical literature, the amount and quality of chemical publication in the various countries of the world, and the relative importance of the several languages employed. Another point of interest is the effect of the two world wars on scientific activity in the different countries and on the languages used for publication (*1*). Studies have been made by various investigators in years past (*1–16*), but the very nature of the problem requires periodic investigation to obtain a clear picture of the trends.

Perhaps the easiest way to study a problem of this sort is to make a statistical analysis of the articles abstracted by leading abstract journals. Since the time involved in such a study is considerable, it is necessary to narrow the field covered, by choosing one specific field of chemistry. Thus it was decided to investigate organic chemistry and to collect data from the Organic Section of *Chemical Abstracts* at intervals as far back as its beginning in 1907 and also to collect data at intervals from the Organic Section of *Chemisches Zentralblatt* from 1907 back to 1877.

The years chosen were 1949, 1948, 1947, 1937, 1927, 1917, and 1907 from *Chemical Abstracts*; and 1907 (for comparison), 1897, 1887, and 1877 from *Chemisches Zentralblatt*. The 1877 data indicated that inclusion of 1867 data would add nothing to the general picture.

Collection of Data

The data collected included name of journal, years in which the journal was published, country of publication, language of the article abstracted (in the case of a polylingual journal the language was determined whenever possible), total number of journals, and total number of abstracts, by country and language (Figs. 1–4). Abstracts of obituary notices and polemic discussions were omitted from the count.

A statistical analysis is not entirely satisfactory, although it seems to be the only practical way to attack the problem. One objection is that it puts a premium on quantity of production, rather than quality. A particular journal may publish many relatively unimportant articles and be considered "important" from a quantitative viewpoint, whereas a second journal, of universally recognized importance, limits itself to publication of a few articles of definite value and suffers from quantitative comparison with the first. However, in a study such as this, which covers a relatively long span of years, the journals of lesser importance may show a good record for a time but tend to fall by the wayside eventually.

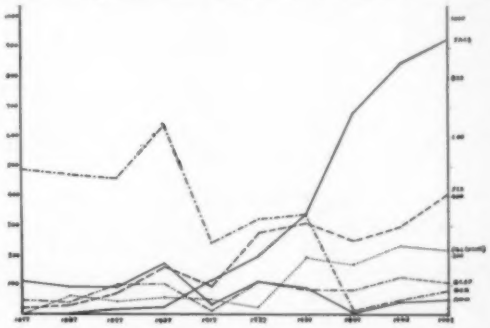

FIG. 1. Production of leading journals (number of abstracts).

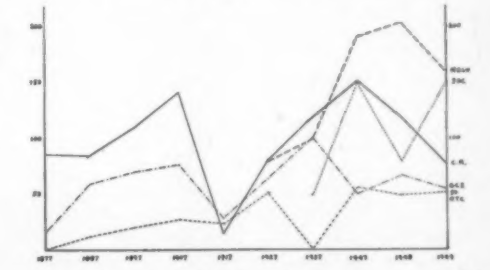

FIG 2. Production of other journals (number of abstracts).

To forestall possible criticism as to the usefulness of quantitative surveys of scientific literature as compared with qualitative analyses, Margery Bedinger

[1] Based on an address presented at the joint meeting of the History of Chemistry and Chemical Literature sections, Chicago meeting of the American Chemical Society, Sept. 3–8, 1950.

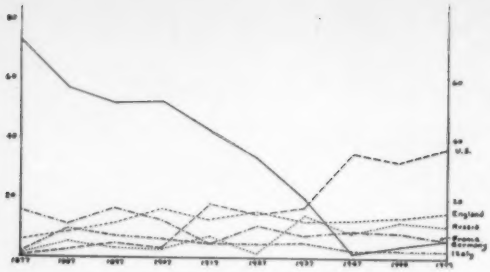

FIG. 3. Percentage of abstracts by country.

FIG. 4. Percentage of abstracts by language.

(*17*), head of the Science and Engineering Department of the Denver Public Library, was asked for her opinion on this point. Her reply indicated that, since the potential number of requests for a journal will be a function of the number of papers appearing in it, the value of a quantitative analysis would seem to be self-evident. "Our budgets are always limited and we are forced to make a selection, choosing what periodicals we subscribe to carefully. In this difficult choice, amount of use is a very important factor" (*17*).

A second objection to a statistical analysis is the problem of availability of some journals for abstracting. However, the importance of a journal is measured at least partially by its availability, regardless of the quality of its content. This, of course, borders on the philosophical and leaves much room for argument. In the early years of *Chemical Abstracts* the coverage was naturally not as complete as the long-established *Chemisches Zentralblatt*, but today *Chemical Abstracts* is recognized to be the most complete of the abstracting journals. In spite of this, the coverage in some areas, and notably in the case of Russian publications, is incomplete (*1, 16, 18, 19*). In the earlier years *Chemisches Zentralblatt* did not cover the field thoroughly, for a close analysis of the abstracts reveals that certain foreign journals of importance were very poorly covered, whereas the native German publications were exhaustively abstracted. This situation, of course, leads to a slightly distorted picture in the earlier years of this study.

The data have been assembled in 5 tables and accompanying graphs, which indicate the situation very clearly. Table 1 lists the most heavily abstracted journals, their years of publication, the number of abstracts from each journal in each of the years studied, and their relative importance from a quantitative viewpoint, as well as the total number of contributing journals and the total number of abstracts for each of the years studied. Table 2 gives an analysis of the number of abstracts by country of publication, and Table 3, by language of publication. Table 4 presents the data in terms of percentages by country, and Table 5, in terms of percentages by language.

Herman H. Fussler (*11*), director of the University of Chicago libraries, surveyed the literature used by chemists and physicists, tabulating the references cited by the authors of papers published in *Physical Review* and the *Journal of the American Chemical Society*. The results obtained agree in general with our observations, except that the Russian journals suffer in Dr. Fussler's survey, probably because of the language barrier.

Interpretation of the Data

Table 1 shows that, of the leading 15 journals in 1949, six were in the first ten in 1877, whereas six are "newcomers" in the past twenty years or so. Four of the first ten in 1877 have been discontinued or have had a change of name. *Journal of the American Chemical Society* had no abstracts in *Chemisches Zentralblatt* in 1877 or 1887, but in 1897 it was in eighteenth position and by 1917 was second in *Chemical Abstracts*. In 1937 it was tied with the German *Berichte*, but since World War II it has gone far out in front. *Journal of the Chemical Society* of London was eighth in *Chemisches Zentralblatt* in 1877, gradually increased in importance, and attained second place in *Chemical Abstracts* in 1927, where it is at present. *The Journal of General Chemistry USSR* started publication in 1931 and has risen rapidly to third place. *Helvetica Chimica Acta* of Switzerland started publication in 1918 and rapidly assumed a leading position in the field, now being a fixture in fourth place. The American *Journal of Organic Chemistry* (1936) has had a rapid growth and is now in fifth place. *Bulletin of the Chemical Society of France* (1858) had already demonstrated its importance by 1877 (fourth) and has retained its importance despite declines in two world wars. The *Berichte* of Germany (1867) was the leader in 1877 and retained this lead even during the first world war, was tied in 1937 by the *Journal of the American Chemical Society*, then suffered a catastrophic decrease during the second world war but has since climbed to seventh position. The *Comptes rendus* of France is primarily a general science journal but has been an important contributor ever since it started publication in 1835. Other important journals of long standing include *Nature, Gazzetta chimica italiana, Recueil des travaux chimiques* (Holland), the well-known *Annalen*, and the Austrian *Monatshefte*. Important newcomers include *Doklady Akademii Nauk SSSR*, the American

TABLE 1

NUMBER OF ABSTRACTS BY PERIODICALS

Journal	Years	*Chemical Abstracts*												*Chemisches Zentralblatt*							
		1949		1948		1947		1937		1927		1917		1907		1907		1897		1887		1877	
J. Am. Chem. Soc.	1876–	1	927	1	848	1	682	1†	337	3	196	2	115	12	18	18	23	17	17	—	0	—	0
J. Chem. Soc. (London)	1847–	2	406	2	297	2	254	3	307	2	278	3	94	5	88	4	160	6	70	11	29	8	19
J. Gen. Chem. USSR	1931–	3	219	3	233	5	170	4	213	—	—	—	—	—	—	—	—	—	—	—	—	—	—
Helv. Chim. Acta	1918–	4	160	4	203	4	190	7	98	7	78	—	—	—	—	—	—	—	—	—	—	—	—
J. Org. Chem.	1936–	5	150	10	79	7	149	12	49	—	—	—	—	—	—	—	—	—	—	—	—	—	—
Bull. soc. chim. France	1858–	6	107	6	126	8	81	9	83	5	109	11	13	4	97	6	104	3	100	8	40	4	42
(Chem.) Berichte	1867–	7	79	13	51	25	15	1†	337	1	321	1	240	1	539	1	637	1	456	1	468	1	486
Compt. rend.	1835–	8	77	7	118	6	151	5	118	6	80	9	15	3	125	5	141	2	109	3	84	3	85
Nature	1869–	9	72	9	80	13	41	25	19	—	6	—	0	—	0	—	0	—	0	—	0	—	0
Doklady Akad. Nauk SSSR	1933–	10	64	23	22	—	0	—	0	—	—	—	—	—	—	—	—	—	—	—	—	—	—
Gazz. chim. ital.	1871–	11	55	11	67	12	50	6	100	9	64	6	28	13	12	7	76	7	69	7	58	9	16
Rec. trav. chim.	1882–	12	52	14	49	11	56	—	0	12	52	7	23	11	25	17	27	16	20	—	12	—	0
Annalen	1832–	13	48	15	42	—	3	8	88	4	110	5	32	6	81	3	172	4	91	2	93	2	107
Org. Syntheses	1921–	14	45	—	1	16	28	20	30	17	30	—	—	—	—	—	—	—	—	—	—	—	—
Izvest. Akad. Nauk SSSR		15	44	8	88	—	0	—	0	—	—	—	—	—	—	—	—	—	—	—	—	—	—
J. Biol. Chem.	1905–	16	44	19	30	14	36	13	46	15	44	10	15	—	0	—	13	—	—	—	—	—	—
Monatshefte	1880–	17	41	24	22	—	9	—	15	11	61	12	11	9	37	8	70	14	29	9	40	—	—
J. Applied Chem. (USSR)	1928–	18	41	20	28	19	25	14	43	—	—	—	—	—	—	—	—	—	—	—	—	—	—
Acta Chem. Scand.	1947–	19	40	25	21	—	0	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
Ind. Eng. Chem.	1909–	20	40	16	41	10	63	—	10	—	8	—	1	—	—	—	—	—	—	—	—	—	—
J. Indian Chem. Soc.	1924–	21	39	12	55	17	27	15	38	14	46	—	—	—	—	—	—	—	—	—	—	—	—
Proc. Indian Acad. Sci.	1924–	22	36	21	25	26	15	—	15	—	0	—	—	—	—	—	—	—	—	—	—	—	—
Can. J. Research	1929–	23	32	17	37	22	19	—	10	—	—	—	—	—	—	—	—	—	—	—	—	—	—
J. Soc. Chem. Ind. Japan	1898–	25	23	5*	128	—	0	—	16	—	9	—	0	—	0	—	0	—	—	—	—	—	—
Collection Czech. Chem. Communs.	1929–	28	17	18	34	—	5	—	11	—	—	—	—	—	—	—	—	—	—	—	—	—	—
J. Chem. Soc. Japan	1880–	—	10	—	2	3*	219	21	19	—	1	—	0	—	1	—	0	—	0	—	0	—	—
Bull. Chem. Soc. Japan	1926–	—	2	—	8	9*	75	19	30	16	31	—	—	—	—	—	—	—	—	—	—	—	—
Arkiv Kemi, Mineral. Geol.	1902–	—	9	—	17	15	31	—	9	—	2	—	1	—	0	—	5	—	—	—	—	—	—
Compt. rend. acad. sci. URSS	1828–	—	2	—	13	18	26	—	17	—	0	—	0	—	0	—	0	—	0	—	0	—	0
Anales fis. y quim.	1902–	—	6	—	14	20	23	—	2	—	4	—	3	—	0	—	0	—	—	—	—	—	—
Z. physiol. Chem.	1877–	—	4	—	2	—	5	16	38	8	77	—	1	—	1	11	50	—	6	—	6	—	0
J. prakt. Chem.	1834–	—	0	—	0	—	0	11	60	10	61	8	22	8	39	9	61	5	77	4	70	6	30
J. Pharm. Soc. Japan	1881–	—	0	—	0	—	0	10	71	13	47	13	11	—	0	—	0	—	0	—	0	—	—
J. Russ. Phys. Chem. Soc.	1869–1930	—	—	—	—	—	—	—	—	18	25	4	54	7	69	10	57	10	41	6	62	—	0
Roczniki Chem.	1921–39	—	5	—	9	—	0	17	37	25	13	—	—	—	—	—	—	—	—	—	—	—	—
Proc. Chem. Soc. (England)	1841?–?	—	—	—	—	—	—	—	—	—	0	—	0	2	146	2	180	8	63	—	0	—	0
American Chem. J.	1879–1914	—	—	—	—	—	—	—	—	—	—	—	—	10	27	15	37	9	50	10	31	—	—
Chem. News	1859–1932	—	—	—	—	—	—	—	—	—	4	—	2	—	2	—	7	13	32	5	63	5	32
Sitzber. Akad. Wiss. Wien	1848–1923	—	—	—	—	—	—	—	—	—	—	—	0	—	1	—	0	—	1	—	0	7	21
Total journals			235		236		205		222		148		50		53		110		93		94		30
Total abstracts			3,530		3,388		2,961		3,048		2,119		785		1,402		2,364		1,542		1,303		904

* These figures represent a six-year period, 1941–46.
† Tied.

TABLE 2

NUMBER OF ABSTRACTS BY COUNTRY

	Chemical Abstracts												*Chemisches Zentralblatt*							
	1949		1948		1947		1937		1927		1917		1907		1907		1897		1887		1877	
United States	1	1302	1	1101	1	1057	2	524	3	307	2	141	5	53	5	86	5	76	7	35	7	6
England	2	550	2	462	2	374	4	369	2	331	3	101	2	240	2	382	3	175	4	110	3	53
Russia	3	386	3	422	5	250	3	432	10	41	4	57	4	75	7	67	6	50	5	67	6	9
France	4	225	4	285	4	267	5	232	4	219	6	38	3	236	3	288	2	250	2	142	2	137
Germany	5	219	7	147	10	57	1	611	1	714	1	336	1	736	1	1232	1	801	1	747	1	654
Switzerland	6	185	5	216	6	204	9	99	7	78	—	—	—	2	—	4	—	3	—	5	—	2
India	7	138	8	118	8	74	8	103	9	50	—	—	—	—	—	—	—	—	—	—	—	—
Japan	8	97	6	175	3*	329	6	205	5	116	8	16	—	3	—	—	—	1	—	—	—	—
Italy	9	92	9	93	7	76	7	156	6	97	7	38	8	12	4	144	4	109	3	119	5	16
Sweden	10	73	11	51	11	39	17	15	13	8	9	6	—	—	—	6	—	—	—	—	—	—
Holland	11	62	10	55	9	62	10	67	8	63	5	42	6	29	8	39	8	26	8	13	—	—
Canada	12	33	12	40	14	20	19	12	18	4	—	1	—	—	—	—	—	—	—	—	—	—
Spain	13	20	14	25	12	36	22	7	19	4	10	3	—	—	—	—	—	—	—	—	—	—
Belgium	14	17	21	11	16	12	15	18	11	35	—	—	7	12	9	23	9	14	11	3	—	—
Czechoslovakia	15	17	13	37	17	6	13	21	—	2	—	—	—	—	—	—	—	2	9	8	—	—
China	16	14	16	19	—	1	12	35	—	—	—	—	—	—	—	—	—	—	—	—	—	—
Poland	17	14	15	20	—	6	11	53	—	17	—	—	—	—	10	10	—	—	—	—	—	—
Rumania	18	14	—	6	—	0	—	3	17	5	—	—	—	2	—	3	—	1	—	—	—	—
Argentina	19	9	17	16	—	5	20	8	—	2	—	—	—	—	—	—	—	—	—	—	—	—
Mexico	20	8	—	4	—	4	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
Brazil	21	6	—	3	—	3	—	1	—	—	—	—	—	—	—	—	—	—	—	—	—	—
Ireland	22	5	—	3	—	—	—	1	—	2	11	3	—	—	—	—	—	—	—	—	—	—
Australia	23	4	19	14	—	5	21	8	21	2	—	—	—	—	—	—	—	—	—	—	—	—
Austria	24	4	—	1	15	12	14	19	14	7	—	—	—	1	6	77	7	30	6	49	4	27
Hungary	25	4	22	11	—	5	18	13	—	—	—	—	—	—	—	—	—	—	—	—	—	—
Finland	26	3	18	16	13	32	16	15	16	6	—	2	—	—	—	—	10	3	—	—	—	—
Jugoslavia	27	3	20	14	—	—	—	3	—	—	—	—	—	—	—	—	—	—	—	1	—	—
Israel	28	2	—	1	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
Turkey	—	2	24	5	—	3	—	2	—	—	—	—	—	—	—	—	—	—	—	—	—	—
Uruguay	—	2	—	—	—	—	—	1	—	—	—	—	—	—	—	—	—	—	—	—	—	—
Norway	—	1	—	2	—	2	—	3	—	—	—	—	—	—	—	—	—	—	—	—	—	—
Peru	—	1	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
Siam	—	1	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
Denmark	—	0	—	4	—	1	—	—	—	—	—	—	—	—	—	1	—	1	—	—	—	—
Bulgaria	—	0	—	3	—	0	—	2	—	—	—	—	—	—	—	—	—	—	—	—	—	—
Philippines	—	—	—	—	—	—	—	2	15	7	—	—	—	—	—	2	—	—	—	—	—	—
Total abstracts		3,530		3,388		2,961		3,048		2,119		785		1,402		2,364		1,542		1,303		904
Total countries		33		36		31		35		24		13		13		15		15		12		8

* These figures represent a six-year period.

TABLE 3

TABLE 3

NUMBER OF ABSTRACTS BY LANGUAGE

	Chemical Abstracts										*Chemisches Zentralblatt*									
	1949		1948		1947		1937		1927		1917		1907		1907		1897		1887		1877	
	1	2169	1	1804	1	1691	1	1098	1	811	2	252	2	296	2	470	3	257	3	149	3	59
English	2	391	4	344	3	305	2	773	2	804	1	338	1	737	1	1326	1	837	1	805	1	687
German	3	386	2	409	3	222	3	395	6	33	3	57	4	75	5	67	5	50	5	62		0
Russian	4	293	3	373	4	339	4	201	3	360	5	38	3	230	3	315	2	277	2	152	2	142
French	5	94	6	95	6	76	6	156	4	98	6	38	6	12	4	144	4	109	4	119	4	16
Italian																						
Japanese	6	88	5	164	4	238	5	171	5	62	7	11		1								
Spanish	7	87	8	46		48	10	17	10	6	9	3										
Polish	8	40	7	20			7	38	7	9		6										
Swedish	9	14	8	11	10	8	8	13	8	8	8	7				1						
Dutch	10	7		5	9	10	9	8	9	24	4	11	5	29	6	38	6	10	7	6		
Portuguese			6	4		3		1														
Hungarian			4	11		5	11	12														
Chinese			2	4		0		6														
Hebrew			2											2		2						
Rumanian			2							5												
Finnish			1	7	8	11																
Norwegian			1	1		1													8	1		
Serbian (Croatian)			1	12																		
Turkish			1	4		0										1						
Danish			0	4		1																
Czech			0	3		3	12	10								7		2	6	8		
Bulgarian			0	3		0		23														
Ukrainian							9	23														
Greek								1														
Lettish																						
Total languages		19		20		15		22		14		9		8		9		7		8		4
Total abstracts		3,530		3,988		2,961		3,048		2,119		785		1,402		2,364		1,542		1,303		904

Organic Syntheses (1921), and the *Journal of Biological Chemistry* (1905).

A glance at the figures in Table 1 will show that there is now about 50 per cent more publication in organic chemistry than in 1907, and the number of contributing journals has greatly increased. Publication was drastically curtailed during both wars, although the decline in World War II is masked in the figures for 1947 because publication in the United States increased tremendously and, also, at this time *Chemical Abstracts* was busily engaged in bringing up to date the abstracting of Japanese and Italian wartime publications covering a six-year period (*1*). These two factors almost compensated for the decreased publication in countries affected by the war, principally Germany, Russia, and Italy. Table 1 has been compiled with the 23 leading publications in 1949 listed in order. Beginning with the *Journal of the Society of Chemical Industry of Japan*, 16 additional journals are listed which have enjoyed a measure of importance at some time in the past.

Analysis of Table 2, showing the relative importance of publication by countries through the years, reveals the rapid growth of publication in the United States, from seventh in 1877 to second in 1917 and 1937, and first since 1947. Germany was the undisputed leader even during the first world war, when its output declined considerably but not quite enough to lose first place. The second world war, however, put an end to German leadership, and in 1949 it had come back to only fifth place. England and France have consistently held leading positions, and since 1927 Russia has rapidly forged ahead into third place in spite of admittedly incomplete coverage (*1, 16, 18, 19*), for which the Russian government is directly responsible.

Table 3, showing the number of abstracts by language, indicates that German was the leading language until shortly after the first world war, when English took the lead. Reference to Table 3 indicates that no Russian articles were abstracted in the 1877 *Chemisches Zentralblatt*, but by 1887 Russian was in fifth place among the languages, although it did not rate too highly from the standpoint of number of abstracts. The two world wars resulted in a decrease in Russian publication, but now it appears to be running a close race with German for second place. The French language was at one time second in importance, with German in the lead, but it was first displaced by English and then by Russian, so that today it ranks fourth. The increasing importance of the Russian language is a point which universities should note, with regard to language requirements for the Ph.D. degree. Only a few universities accept Russian in partial fulfillment of the language requirements for that degree, yet Russian is as useful to a chemist as French where current literature is concerned.

The Italian language has been of importance to the scientific world. In 1877 it was fourth, continuing in fourth place until the first world war, when it dropped to sixth place. At the present time it is competing

TABLE 4

PERCENTAGE OF ABSTRACTS BY COUNTRY

	Chemical Abstracts							*Chemisches Zentralblatt*			
	1949	1948	1947	1937	1927	1917	1907	1907	1897	1887	1877
United States	1 37.0	1 32.5	1 35.6	2 17.1	3 14.5	2 18.0	5 3.9	5 3.6	5 4.9	7 2.7	7 0.7
England	2 15.6	2 13.6	2 12.6	4 12.1	2 15.6	3 12.9	2 17.1	2 16.2	3 11.4	4 8.5	3 5.9
Russia	3 10.9	3 12.4	5 8.4	3 14.2	10 1.9	4 7.3	4 5.4	7 2.8	6 3.2	5 5.2	6 1.0
France	4 6.4	4 8.4	4 9.0	5 7.6	4 10.7	6 4.8	3 16.8	3 12.2	2 16.2	2 10.9	2 15.2
Germany	5 6.2	7 4.3	10 1.9	1 20.0	1 33.7	1 42.8	1 52.5	1 52.1	1 52.0	1 57.1	1 72.4
Switzerland	6 5.2	5 6.4	6 7.0	9 3.3	7 3.7	— —	— 0.1	— 0.2	— 0.2	10 0.4	8 0.2
India	7 3.9	8 3.5	8 2.5	8 3.4	9 2.4	— —	— —	— —	— —	— —	— —
Japan	8 2.7	6 5.2	3 11.1	6 6.7	5 5.5	8 2.0	— 0.2	— —	— —	— —	— —
Italy	9 2.6	9 2.7	7 2.6	7 5.1	6 4.6	7 4.8	8 0.9	4 6.1	4 7.1	3 9.2	5 1.8
Sweden	10 2.1	11 1.5	11 1.3	— 0.5	— 0.4	9 0.7	— —	— 0.3	— —	— —	— —
Holland	11 1.8	10 1.6	9 2.1	10 2.2	8 3.0	5 5.4	6 2.1	8 1.7	8 1.7	8 1.0	— —
Canada	12 0.9	12 1.2	14 0.7	— 0.4	— 0.2	— 0.1	— —	— —	— —	— —	— —
Spain	13 0.6	14 0.7	12 1.2	— 0.2	— 0.2	10 0.4	— —	— —	— —	— —	— —
Belgium	14 0.5	— 0.3	— 0.4	15 0.6	11 1.7	— —	7 0.9	9 1.0	9 0.9	11 0.2	— —
Czechoslovakia	15 0.5	13 1.1	— 0.2	13 0.7	— 0.1	— —	— —	— —	— 0.1	9 0.6	— —
China	— 0.4	16 0.8	— —	12 1.1	— —	— —	— —	— —	— —	— —	— —
Poland	— 0.4	15 0.8	— —	11 1.6	12 0.8	— —	— —	10 0.4	— —	— —	— —
Rumania	— 0.4	— 0.2	— —	— —	— 0.2	— —	— 0.1	— 0.1	— —	— —	— —
Austria	— —	— —	— —	14 0.6	— 0.3	— —	— —	6 3.2	7 1.9	6 3.8	4 3.0

TABLE 5

PERCENTAGE OF ABSTRACTS BY LANGUAGE

	Chemical Abstracts							*Chemisches Zentralblatt*			
	1949	1948	1947	1937	1927	1917	1907	1907	1897	1887	1877
English	1 61.2	1 55.0	1 57.0	1 36.1	1 38.4	2 32.1	2 21.1	2 19.9	3 16.7	3 11.5	3 6.5
German	2 11.0	4 10.2	3 10.3	2 25.4	2 37.0	1 43.1	1 52.5	1 56.0	1 54.1	1 61.8	1 76.1
Russian	3 10.9	2 12.1	5 7.5	3 12.9	6 1.6	3 7.3	4 5.4	5 2.8	5 3.2	5 4.8	— 0
French	4 8.2	3 11.0	2 11.4	4 9.9	3 12.3	5 4.8	3 17.8	3 13.3	2 19.0	2 11.7	2 15.7
Italian	5 3.3	6 2.8	6 2.6	6 5.1	4 4.6	6 4.8	6 0.9	4 6.1	4 7.1	4 9.2	4 1.8
Japanese	6 3.1	5 4.8	4 8.0	5 5.6	5 2.9	7 1.4	— —	— —	— —	— —	— —
Spanish	7 1.1	7 1.4	7 1.6	10 0.6	10 0.3	9 0.4	— —	— —	— —	— —	— —
Polish	8 0.4	8 0.6	— —	7 1.2	7 0.7	— —	— —	— —	— —	— —	— —
Swedish	9 0.3	10 0.3	10 0.3	13 0.3	9 0.3	8 0.8	— —	— —	— —	— —	— —
Dutch	10 0.2	11 0.1	9 0.3	8 0.8	8 0.5	4 5.4	5 2.1	6 1.6	6 0.7	7 0.5	— —
Portuguese	11 0.2	12 0.1	— 0.1	— —	— —	— —	— —	— —	— —	— —	— —
Hungarian	12 0.1	9 0.3	— 0.1	11 0.4	— —	— —	— —	— —	— —	— —	— —

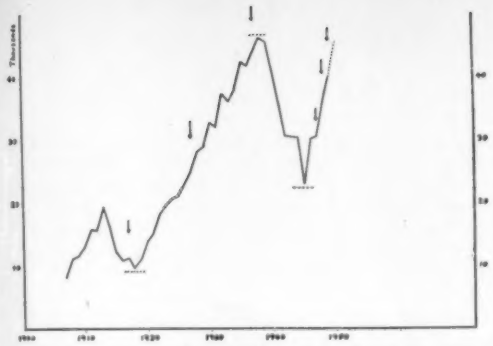

FIG. 5. Abstracts of papers vs years. (From E. J. Crane. *Chem. Eng. News*, **27**, 529 [1949]).

with Japanese for fifth place. The Japanese language is the only other language of importance.

Contributions by country and by language have also been investigated from the standpoint of percentage of total output. These figures are given in Table 4, which shows percentages of all abstracts by country, and also in Table 5, which presents percentages of all abstracts by language. These figures have also been interpreted by means of graphs, which indicate clearly the changes in relative importance since 1877.

Fig. 3 reveals how the importance of Germany as a publisher of scientific articles in the field of organic chemistry has decreased and how that of the United States has risen. Fig. 4 exhibits conclusively the decline of German as a scientific language and the rapid increase in importance of the English language, which in 1949 accounted for over 60 per cent of all articles abstracted in *Chemical Abstracts*. Similarly, as in Fig. 3, Russian shows increased importance, whereas French and Italian show corresponding decreases.

In order to obtain a clearer picture of how total publication (total abstracts for *all* fields) has developed over the years, Fig. 5 has been included. This has been borrowed from E. J. Crane (*9, 10*). The general decline in total publication during 1913–18 was followed by a period of increased productivity until the peak year of 1938. A steady decline in productivity followed, reaching its low point in 1945. Since 1945 a sharp increase in publication has taken place, and there is a possibility that in 1950 the peak of 1938 may have been reached.

CONCLUSIONS

From the data collected, it appears that the ten leading journals in the field of organic chemistry at the present time (from a total production standpoint) are, in order: *Journal of the American Chemical Society* (1876), *Journal of the Chemical Society* (1847), *Journal of General Chemistry of the U.S.S.R.* (1931), *Helvetica Chimica Acta* (1918), *Journal of Organic Chemistry* (1936), *Bulletin of the Chemical Society of France* (1858), *Chem. Berichte* (1867), *Comptes rendus* (1835), *Nature* (1869), and *Doklady Akad. Nauk S.S.S.R.* (1933). In 1877 four of these journals were in the leading ten: *Journal of the Chemical Society, Bulletin of the Chemical Society of France, Chem. Berichte,* and *Comptes rendus.*[5]

An analysis of countries contributing to the literature of organic chemistry shows that the five leaders are now the United States, England, Russia, France, and Germany. In 1877 the order was Germany, France, England, Austria, and Italy. The United States was seventh at that time. In 1897 the United States was fifth, second in 1937, and has been first since 1947.

An analysis of languages of publication reveals that the languages in order of importance are now English, German, Russian, French, and Italian. In 1877 the order was German, French, English, and Italian.

Graphical representation, where percentage of total abstracts by country and language are plotted against years, reveals that about 1927 the English language replaced German as the leading language in the field of organic chemistry, and about 1938 the United States took over the lead in publication from Germany.

Investigation of total publication in *all* fields of chemistry reveals that world publication fell off from 1913–18 during the first world war, then increased until the peak year of 1938, and then rapidly declined during the period of the second world war from 1938–45. Since 1945 there has been a steady increase in world publication, and estimated figures for 1950 show that the 1938 total may have been reached in that year.

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News and Notes

Ceylon Meeting of FAO

A REGIONAL conference on land utilization in tropical areas of Asia and the Far East was held in Ceylon, Sept. 15–29. Participating were 75 administrators, agronomists, economists, engineers, foresters, and soil scientists from FAO and from 14 countries, including Australia, Belgium, Burma, Cambodia, Ceylon, France, India, Indonesia, The Netherlands, Pakistan, Portugal, the United Kingdom, Vietnam, and the United States. Delegates from the U. S. were Tom Gill, of the Society of American Foresters, chairman; Milton H. Button, agricultural officer for Trust Territories of the Pacific Islands; Raymond H. Davis, ECA; Harold B. Donaldson, Natural Resources Section, SCAP; and Robert L. Pendleton and Roy W. Simonson, USDA.

The discussions, held in Nuwara Eliya, covered three main topics: (1) determining optimum use of tropical land resources, (2) achieving optimum and preventing undesirable uses, (3) improving and maintaining productivity of tropical lands.

Much emphasis was given to the need for proper classification and mapping of tropical lands as part of the process of determining optimum use. Mapping activities believed necessary range from aerial photography to detailed soil and forest surveys. The series of steps outlined to provide for appraisal of potentialities of tropical lands were, first, the delineation of broad regions generally similar in their patterns of vegetation, soils, and geology; second, more precise outlining of the kinds and distribution of soils; and, third, the determination of use-capabilities of soils from available experience and research findings. As a basic principle, it was urged that governments obtain comprehensive summaries of facts about land and water resources before plans for development are made, and that these fundamental facts should then be employed as essential tools in the planning process. It was recognized that additional research on fundamental properties of soils in tropical regions was essential for determining their best use. Experience with direct application of methods used successfully in temperate zones has not been happy generally. Special efforts seem necessary in some countries to correct the widespread practice of shifting cultivation, with its harmful effects on forest resources. The development of alternative means of obtaining a livelihood may be necessary to stop shifting cultivation.

The discussions during the eight days of the conference touched many other topics, which can be illustrated by mention of a few. Briefly considered were the effect of agricultural price policies on land use, better coordination of research on land and water utilization in the institutions of Asia and the Far East, the adoption by each country of a sound forest policy, the establishment and care of communal forest plots near villages, the control and eradication of *Imperata cylindrica*, the fragmentation of peasant holdings, and the possible use of *Sesbania speciosa* as a green manure crop on rice paddies. This list suggests the variety of topics involved in any comprehensive discussion of land utilization.

A four-day field tour, sponsored by the host government, gave delegates an opportunity to see irrigation and dry-farming development schemes in the "dry zone" of Ceylon, the ruins of cities and irrigation works that flourished centuries ago, and the production of tea in field and factory. In construction of present irrigation systems, the government of Ceylon is able to restore ancient dams and use parts of former canals. The old works thus reduce present costs and are of great value. Efforts to promote dry farming on soils akin to those of the Cross Timbers region of Texas seem a far cry from dry farming in the U. S. The annual rainfall in the dry zone of Ceylon ranges upwards from 40 in., but the comparatively high temperatures throughout the year and the long dry season make the rainfall far less effective than it is in our Great Plains. Much of Ceylon lies in the dry zone, now used only to a limited extent. In the tours, delegates saw plantations and factories producing the tea for which Ceylon is famous. Tea is widely grown on hilly lands at higher elevations, though a few slopes seem poorly adapted to any type of cultivation.

The meeting in Ceylon permitted men from various fields to compare present land utilization in their several countries, to exchange information on methods for improvement that had been successful, and to get acquainted with one another. The field tours provided some common reference points that will be helpful in future discussions and correspondence. Ultimately, the opportunity for a continuing exchange of ideas among men who now know each other may well be as helpful as will the FAO report summarizing discussions at the conference.

ROY W. SIMONSON

Division of Soil Survey, ARA
Beltsville, Maryland

Scientists in the News

Raymond B. Allen, retiring president of the University of Washington, has been named chancellor of the University of California at Los Angeles. Dr. Allen was recently appointed to head the U. S. Psychological Strategy Board, a post he is expected to fill until he takes up his duties in Los Angeles next summer.

Paulo C. A. Antunes, assistant director of the Pan American Sanitary Bureau, Washington, D. C., has resigned to become dean of the School of Hygiene and Public Health, University of São Paulo, Brazil. **M. G. Candau** has been named to replace him. **V. A.**

Sutter, of the WHO headquarters staff, will serve as acting assistant director of the bureau pending the arrival of Dr. Candau in March.

Guy Camus, research fellow in biology at Caltech, has been granted the first award of the Louis Rapkine Foundation of Paris for distinguished work in his specialty. The Rapkine Foundation was established in memory of the French biologist Louis Rapkine, who died in 1949 at the age of 42.

Carl Djerassi, of Syntex Laboratories, Mexico City, has been appointed an associate professor of organic chemistry at Wayne University. Dr. Djerassi was a member of the group of Syntex chemists who recently completed the total synthesis of cortisone.

C. T. Elvey, senior scientist and deputy head of research at the Naval Ordnance Test Station, China Lake, Calif., has been appointed director of the Geophysical Institute of the University of Alaska. Dr. Elvey is an astrophysicist and an authority on the light of the night sky.

A. W. Friend has been named director of engineering and development of Magnetic Metals Company, Camden, N. J. Dr. Friend has been on the staffs of West Virginia and Harvard universities, MIT, RCA, and Daystrom, Inc.

Henry A. Imus, head of the Psychophysiology Branch, Biological Sciences Division, ONR, and now on assignment to the London Branch Office of Naval Research, has recently been elected to membership in the Ergonomics Research Society and in the British Psychological Society.

The University of Louisville School of Medicine has appointed **U. Pentti Kokko** associate professor in child health research. Dr. Kokko will continue studies in poliomyelitis in the school's Kentucky Child Health Foundation Laboratory, which is under the direction of **Alex J. Steigman**, professor of child health.

Oscar Lewis, University of Illinois anthropologist, spoke at the International Congress on Mental Health in Mexico City on "Effects of Technical Progress on Mental Health in Rural Populations." He also led a discussion section on problems of mental health and technological innovations.

D. E. Lindstrom, for 22 years head of rural sociology work in the Illinois College of Agriculture, has been granted a three-year leave of absence to accept appointment in the newly organized International Christian University in Japan, starting in January 1953. He will serve as professor of rural sociology, member of the graduate faculty, and either director or cochairman with a Japanese staff member of a proposed rural community study project.

D. A. A. Mossel, microbiologist in the Central Institute for Nutrition Research, TNO, Utrecht, The Netherlands, is participating in an ECA project on food technology and hygiene and will be in the U. S. during January, February, and March.

Karl S. Quisenberry has been appointed assistant chief in charge of program planning and coordination for the Bureau of Plant Industry, Soils, and Agricultural Engineering, USDA. He succeeds **A. H. Moseman**, who recently became the bureau's chief. Dr. Quisenberry entered the Department of Agriculture in 1925, and from 1936 to 1946 was located at Lincoln, Nebr., in charge of the regional cooperative breeding program for hard red winter wheat and other work on oats, rye, and barley. Since 1946 he has been head of the Division of Cereal Crops and Diseases at Beltsville, Md.

Recent visitors at the ARA Eastern Regional Research Laboratory, Philadelphia, included **V. Ramakrishman**, Madras; **Roy Dru**, consulting chemist, Paris; **Alexander Meller**, Melbourne, Australia; **Ferdinand Sanchez**, Puerto Rico Agricultural Experiment Station, Río Piedras; **M. A. Himmet**, director, Egyptian Government Laboratory, Alexandria; and **Y. Nishisaka**, president, Nishisaka Industry Co., Osaka, Japan.

Samuel Ray Scholes, professor of glass technology in the New York State College of Ceramics, has been named last year's recipient of the Albert Victor Bleininger Award. Dr. Scholes is the fifth recipient of the Bleininger Award, which was established by the Pittsburgh Section of the American Ceramic Society with the purpose of conferring deserved recognition on distinguished men in ceramics.

Gerald Wendt has accepted appointment as head of the Division of Teaching and Dissemination of Science in the Department of Natural Sciences of Unesco. His job at Unesco will entail responsibility for many world-wide programs of public education in science, including traveling exhibits, stimulation of international amateur science clubs, and informational aid to local science organizations scattered around the world. Dr. Wendt will also edit Unesco's quarterly journal, *Impact*.

M. S. White, USAF (MC), formerly air surgeon for the USAF in Europe, was recently appointed air surgeon for the Tactical Air Command. Colonel White served a three-year tour of duty in Europe before his arrival at TAC headquarters at Langley Air Force Base, Va. The post of USAFE air surgeon is now filled by **William H. Powell**, formerly chief of the Directorate of Professional Services, Office of the Surgeon General, USAF. New chief of Preventive Medicine for the Professional Services Division is **Richard L. Schwartz**.

Charles R. Wilke, associate professor of chemical engineering at the University of California, Berkeley, has been chosen by the American Institute of Chemical Engineers as last year's winner of its Junior Award, for outstanding contributions to the literature of chemical engineering.

Education

The **Air Force School of Aviation Medicine** will institute a special course for sanitary and industrial hygiene engineers at Gunter AFB, Montgomery, Ala. Instruction will be provided for both Air Force engineers and civilian consultants. The program begins in February.

Johns Hopkins has begun a course in its adult education branch entitled "The Family's Approach to Investment Securities," designed to teach the small investor how to get the most out of his money, how to protect his savings, and how to increase his capital as safely as he can under the new tax laws. Thirty-eight per cent of the total registration in the new course consists of women.

Lehigh University has appointed two new department heads, effective Feb. 1. Alan S. Foust, professor of chemical engineering at the University of Michigan, will become head of the Department of Chemical Engineering, and Earl J. Serfass, Lehigh professor of chemistry, will become head of the Department of Chemistry.

Robert O'Connor, Leo Weinschel, and George Collentine, Jr., will function as chairmen of the spring clinics of the **Marquette University Medical School,** Milwaukee, scheduled for Mar. 29. The clinics will be sponsored by the Alumni Association of the Medical School.

The **Social Science Research Center** at Cornell is making a study of a thousand patients in tumor clinics and cancer detection centers in New York state to determine what types of people seek early diagnosis of cancer and what types put it off. Data, which will be made available to the state Department of Health Bureau of Cancer Control, will be used to determine type and focus of educational material. Edward A. Suchman, Robin M. Williams, Jr., and Rose K. Goldsen are project directors.

The Medical Units of the **University of Tennessee** have added these new members to the staff: Robert L. Bacon, of Stanford University; Sidney A. Cohn, who recently received his Ph.D. from Brown University; Lew S. Cunningham, former American Cancer Society research fellow at Stanford; and James S. Davis, Ph.D., from the University of Wisconsin.

Wagner College, Staten Island, has established a Department of Bacteriology and Public Health under the chairmanship of Natale Colosi, adding courses to the curriculum and transferring the courses in medical technology to the new department.

The semiannual **Wayne University** "Frontiers in Chemistry" lecture series will open Feb. 18 with Terrell L. Hill as the speaker. Other lecturers will be: Feb. 25, Allen T. Gwathmey; Mar. 10, Wallace R. Brode; Mar. 17, M. S. Newman; Apr. 7, Philip W. West; Apr. 28, Karl Paul Link; May 5, Robert C. Elderfield; May 12, Hans Boogh Jonassen.

Grants and Fellowships

Funds for a **Geer Fellowship** have been given to Cornell by William C. Geer, alumnus who recently established the Laboratory of Rubber and Plastics in the School of Chemical and Metallurgical Engineering (SCIENCE, 114, 313 [1951]). The two-year graduate fellowship will deal with the biochemistry and biophysical chemistry of the eye.

An annual $4,000 **McGill–Arctic Institute Carnegie Fellowship** has been established at McGill University for senior candidates who have engaged in suitable arctic or subarctic field projects. Applications for 1952–53 should reach Montreal by *May 1* and should be submitted to the secretary of the Carnegie Arctic Program, Arctic Institute of North America, 3485 University St., Montreal, P. Q.

The **National Association for Mental Health,** 1790 Broadway, New York 19, will award a prize of $1,000 for the best report of clinical research that will advance knowledge and understanding of adolescents and of the ways in which they can be helped in their social and emotional adjustment. The award committee consists of George E. Gardner, chairman; Abraham Z. Barhash, Othilda Krug, Fredrick C. Redlich, and Exie E. Welsch. Entries will be due on *June 30,* and the prize will be awarded in February 1953.

Nineteen research and teaching fellowships have been awarded by the **National Tuberculosis Association,** bringing to 43 the number granted since the initiation of the program in 1948. Graduate, undergraduate, and teaching-resident fellowships are included in the program, which is supported by the sale of Christmas Seals, except for three, which have been made possible by memorial gifts.

Playtex Park Research Institute has awarded a three-year grant to the Children's Hospital of Michigan, in Detroit, for the purpose of aiding research in iron metabolism, prevention of iron-deficiency anemia, the anemia of infection in early life, and other phases of hematology. Wolf W. Zuelzer, director of laboratories, will be in charge, and Julius Rutzky will carry on the research.

The **Textile Research Institute** offers four fellowships for graduate study at Princeton University, three in the Department of Chemistry and one in the Department of Chemical Engineering. The institute is a cooperative, industry-supported organization engaged in fundamental research in the physics and chemistry of fibrous materials and other high polymers. Full information may be obtained from J. H. Dillon, Director, Box 625, Princeton, N. J.

The **Van Meter Prize Award,** offered by the American Goiter Association for the best essays concerning original work on problems related to the thyroid gland, will be given at the annual meeting of the association in St. Louis May 1–3. Further information concerning the contest, which closes *Mar. 1,*

may be obtained from George C. Shivers, 100 E. St. Vrain St., Colorado Springs.

In the Laboratories

Armour Research Foundation of Illinois Institute of Technology has appointed Cecil Schwartz, stress analyst, as associate engineer in the heat-power research department. Albert Wienstock, chemist for the Quartermaster Subsistence Testing Laboratory, has been appointed an associate chemist in the chemistry and chemical engineering research department.

Arthur D. Little, Inc., has added Charles McGee, chemist and electrical engineer, formerly of the National Chemistry Laboratory, Poona, India, to its staff. Under a Point IV program the Cambridge research and engineering firm is making an extensive study of raw materials available in Egypt for low-cost housing. Charles G. Harford and Earl Stafford are making the survey.

Construction of the $8,000,000 addition to **Roswell Park Memorial Institute** at Buffalo, N. Y., begun last summer, is expected to be completed in July 1953. The state-owned institution for diagnosis, treatment, prevention, education, and research is one of the four U. S. hospitals approved for a full three-year residency in x-ray therapy.

Schwarz Laboratories, Inc., of New York, is investigating the biochemical properties of glutathione, under an ONR contract. Previous studies have indicated that this compound may have a prophylactic action against radiation in certain animals.

Meetings and Elections

Newly elected officers of the **American Anthropological Association** are: Wendell C. Bennett, president; William Lessa, secretary; J. O. Brew, treasurer; and B. Irving Rouse and Gordon Willey, Executive Board members.

The **American College of Surgeons,** meeting in San Francisco in November, chose Harold L. Foss as president-elect, succeeding Alton Ochsner, who became president. Henry W. Cave is retiring president. Robert H. Kennedy and Thomas F. Mullen were elected vice presidents, William L. Estes, Jr., was re-elected chairman of the Board of Governors, and Robert M. Zollinger was elected vice-chairman.

The **American Society of Anesthesiologists** elected the following officers at its meeting in Washington, D. C.: president-elect, Ralph Knight; vice presidents, B. B. Sankey and Clayton Wangeman. C. Walter Metz was installed as president, succeeding Urban H. Eversole, and J. Earl Remlinger, Jr., and Moses H. Krakow were re-elected secretary and treasurer, respectively.

The **Bureau of Biological Research,** Rutgers, will hold its eighth annual Protein Conference in New Brunswick, N. J., Feb. 1–2. General theme will be the relationships between protein metabolism and the endocrine system. The conference is open to all registrants, and reservation blanks may be secured from William H. Cole, of Rutgers.

George L. Drake has been elected president of the **Society of American Foresters** for a two-year term, succeeding Charles F. Evans. Elwood L. Demmon was elected vice president.

Miscellaneous

Under the Point IV program, the **Caribbean Commission** is sponsoring a vocational training program in Puerto Rico. Thirty students from various Caribbean areas will take one-year courses at the Metropolitan Vocational School in San Juan. Educational expenses of the trainees are being met with the help of a $38,000 grant from the Technical Cooperation Administration.

The **Chekhov Publishing House** has been established by the East European Fund of the Ford Foundation to publish books in Russian for exiles of all Soviet nationalities. These will include prerevolutionary classics and works by contemporary Soviet authors that have been suppressed in the USSR; books by recent exiles and earlier *émigrés*; and translations of books in other languages that best represent Western thought and ways of life. Nicholas Wreden, executive vice president of E. P. Dutton, has been appointed director, and Lilian Plante associate director.

The **National Research Council** has set up in its Division of Biology and Agriculture a Committee on Developmental Biology for a study of development and growth in the broadest sense and to assist in bringing together the many branches of biology bearing on this area, including agricultural sciences, anatomy, physical anthropology, biochemistry, biometrics, cytology, embryology, endocrinology, genetics, histology, microbiology, nutrition, orthopedics, pathology, pediatrics, cellular and general physiology, plant physiology, and radiology. The committee plans to carry out its operations, for which it has received a sizable initial grant, in consultation with investigators, educators, administrators, and societies concerned, and in close liaison with related NRC committees and other agencies. Members of the committee are Paul Weiss, chairman; T. C. Byerly, W. W. Greulich, I. C. Gunsalus, T. M. Sonneborn, K. V. Thimann, and B. H. Willier.

The Office of Scientific Information of the **National Science Foundation** is prepared to support a limited number of carefully selected studies on information needs of scientists and on the effectiveness of present methods and techniques for disseminating information and organizing it for reference purposes. Better understanding of the needs of scientists for information and of the ways in which they use it is a prerequisite to planning effective measures for solving some of the most pressing problems in the field. Inquiries about the program should be submitted to

Robert Tumbleson, Chief, Office of Scientific Information, National Science Foundation, 2144 California St., N.W., Washington 25, D. C.

Recent Deaths

Russell I. Baker (59), chemist, Linden, N. J., Dec. 11; **Thomas H. Bissonnette** (66), biologist, Hartford, Conn., Nov. 30; **Beatrice H. Brickett** (87), physician, Newton, Mass., Dec. 10; **Peter H. Buck** ("Te Rangi Hiroa") (71), anthropologist, Honolulu, Dec. 1; **Arthur E. Davis** (74), cancer specialist, Pittsford, N. Y., Dec 7; **Samuel H. Derickson** (—), biologist, Reading, Pa., Nov. 27; **George E. Doke** (74), mechanical engineer, Yonkers, N. Y., Dec. 6; **James E. A. Eggleson** (72), chemical engineer, Essex Fells, N. J., Dec. 14; **Benjamin K. Fletcher** (83), pediatrician, Philadelphia, Dec. 17; **Edmond Fleutiaux** (94), coleopterist, Nogent-sur-Marne, France, Nov. 25; **W. Wallace Fritz** (81), neuropathologist, Lansdale, Pa., Nov. 24; **Edward T. Grandlienard** (72), civil engineer, Drexel Hill, Pa., Nov 27; **Edgar A. Groves** (69), civil engineer, New York, Nov. 25; **Gene W. Hall** (53), civil engineer, Rockville Centre, N. Y., Nov. 29; **William L. Higgins** (84), physician and civic leader, Norwich, Conn., Nov. 19; **Kirke K. Hoagg** (62), engineer, Scarsdale, N. Y., Dec. 11.

Max Immanuel (61), economist, New York, Dec. 9; **Robert B. Irwin** (68), former executive director, American Foundation for the Blind, Bremerton, Wash., Dec. 12; **Herbert Jackson** (68), botanist, Toronto, Dec. 14; **Carl O. Lampland** (78), astronomer, Flagstaff, Ariz., Dec. 14; **Walter B. Lancaster** (88), ophthalmologist, Boston, Mass., Dec. 9; **John I. Lauritzen** (67), plant physiologist, Riverside, Calif., Nov. 27; **S. G. Law** (49), neuropsychiatrist, Minneapolis, Sept. 3; **N. J. Lennes** (77), mathematician, Missoula, Mont., Nov. 21; **Samuel Levine** (69), internist, Brooklyn, N. Y., Nov. 29; **Andrew F. Lippi** (71), chemist, Philadelphia, Dec. 13; **David McCoach, Jr.** (64), civil engineer, Washington, D. C., Dec. 15; **Carl J. Moroney** (65), engineer and sugar official, San Mateo, Calif., Nov. 27; **Paul H. Musser** (59), educator, Philadelphia, Nov. 21; **Charles F. Noll** (73), agronomist, State College, Pa., Dec. 18.

Charles D. Parfitt (80), of Toronto, tuberculosis specialist, Brookline, Mass., Nov. 20; **Todd M. Pettigrew** (64), geophysicist, Washington, D. C., Dec. 13; **Cesar U. Piedrahita** (64), expert on tropical medicine, Bogota, Colombia, Dec. 17; **Henry S. Raper** (69), physician, Manchester, Eng., Dec. 12; **Jerohn J. Savitz** (85), educator, Westfield, N. J., Dec. 5; **Marc Schuman** (—), inventor, Philadelphia, Nov. 22; **Lemuel F. Smith** (78), chemist, Richmond, Va., Nov. 24; **Angelo L. Soresi** (69), surgeon, Brooklyn, N. Y., Dec. 11; **Leo Spiegel** (72), dermatologist, New York, Dec. 17; **John W. Thomas** (71), chemist and rubber company official, Akron, Ohio, Nov. 26; **Benjamin F. Tillson** (67), mining engineer, Montclair, N. J., Dec. 4; **Theodore P. Walker** (69), industrialist, New York, Nov. 29; **Carl N. Webb** (51), chemist, Oxford, Ohio, Dec. 14; **Archer E. Young** (78), mathematician and research engineer, Mamaroneck, N. Y., Nov. 28.

Technical Papers

The Site of Nitrogen Absorption in Rats Fed Raw and Heat-treated Soybean Meals

R. W. Carroll, G. W. Hensley, and W. R. Graham, Jr.[1]

The Quaker Oats Company Research Laboratories, Chicago, Illinois

It is well known that moderate heat treatment improves the nutritive quality of the proteins of soybeans. Several heat-labile fractions which inhibit tryptic hydrolysis *in vitro* have been obtained from raw soybeans. Some of these have been shown to retard the growth of chicks, rats, and mice. This work has been comprehensively reviewed by Liener (*1*), Laskowski (*2*), Almquist (*3*), and Griswold (*4*).

We have studied the effect of heating on the digestibility and growth-promoting value of the proteins of soybean meal for the rat. Our results, like those of other investigators (*5–7*), indicate that properly heated meal has only slightly higher digestibility than raw meal and that this digestibility difference is so small it can hardly account for the observed marked difference in growth-promoting value. This was true when digestibility estimations were based on fecal nitrogen excretion. When contents of progressive segments of intestine were studied, it became apparent that with properly heated meal, all, or nearly all, of the nitrogen that is ultimately to be absorbed is absorbed during passage of the meal through the small intestine. However, with the raw meal, much of the nitrogen appears to be absorbed from the large intestine.

Digestibility estimations were made by the chromic oxide indicator method described by Schürch *et al.* (*8*). Briefly, the method involves incorporation of a known amount of a completely indigestible material (Cr_2O_3) in the feed, determination of its concentration in the feces, and determination of the nitrogen content of the feed and of the feces. A coefficient of digestibility for the nitrogen of the feed may then

[1] With the technical assistance of P. R. Stout in statistical interpretation.

TABLE 1

COEFFICIENTS OF DIGESTIBILITY OF SOYBEAN NITROGEN

Estimated from analysis of feces			Estimated from analysis of contents of terminal 20% of small intestine			
Ration No.	564	565	564		565	
Sample fed	Raw	Heated	Raw		Heated	
Rat No.	*Period 1*	*Period 2*	Rat No.		Rat No.	
1	77.7	82.1	14	61.5	28	81.4
	77.1	80.3	13	51.5	40	81.4
	77.6	81.9	27	49.1	29	81.0
			12	45.7	35	79.2
	Period 2	*Period 1*	11	44.3	22	77.5
2	77.4	81.2	39	42.1	34	77.2
	75.7	80.7	32	38.5	10	76.9
	78.7	82.0	38	37.7	23	74.7
			26	31.5		
	Period 1	*Period 2*	16	29.8		
3	74.5	84.1	17	28.7		
	75.5	81.8	19	25.8		
	78.4	81.2	20	24.1		
			15	23.0		
			33	−3.5		
			18	−7.4		
Mean	76.96 ± 1.23[a]	81.70 ± 1.23	Mean	32.65 ± 13.53		78.66 ± 3.08

Coefficient of digestibility	*Mean difference*	*Value of* t	*Probability*
From feces	4.7	7.95	< 0.0001
From intestinal contents	46.0	9.83	< 0.0001

[a] Each fiducial limit at 0.01 level.

be calculated from these data through the use of the two nitrogen to Cr_2O_3 ratios.

Raw full-fat soybeans were steamed and rolled, and hexane was extracted with minimum heating. Portions of the extracted flakes were heat-treated by autoclaving. A series of 12 samples, representing varying degrees of heat treatment from raw to badly damaged, was prepared. Each sample was fed to weanling rats for determination of the growth-promoting value of its proteins. The growth test data will be reported in detail elsewhere. Two of the samples were used in the digestibility studies reported here: the first was the unheated solvent-extracted flakes and will be termed "raw;" the second gave a near-maximum growth-promoting value (with respect to the 12-sample series) for rats in the above growth tests and will be termed "heated." The treatment given this heated sample was 15 min autoclaving at 121° C. The 21-day mean nitrogen efficiency values (g gain in body wt/g nitrogen intake) obtained with *ad lib.* feeding of raw sample ration and heated sample ration were 6.2 ± 2.0[2], and 13.7 ± 2.0, respectively.

The rations fed in the growth and the digestibility studies were identical in their levels of salt mixture, added synthetic B complex vitamins (including choline chloride, 200 mg/100 g), vitamins A and D, and α-tocopherol. The rations fed in growth tests contained ground soybean flakes to supply 1.6% total nitrogen and corn oil to give a total fat level of 10%; the rations fed in digestibility studies contained soybean meal to supply approximately 3.5% total nitrogen, 5% total fat, and 2.0% Cr_2O_3. The remainder of each ration was cornstarch.

Three adult rats were used in the gross digestibility studies. Each was carried through two feeding periods: he was fed raw sample ration during one of the periods and heated sample ration during the other. During each of the two feeding periods, each rat received his respective test ration for at least 2 days before any feces were collected. Three 24-hr collections of feces were made for each rat during each period. Feces were collected on screen in order to minimize contamination with urinary nitrogen. Feces samples were air-dried at room temperature sufficiently for grinding in a mortar. After removal of most of the hair by sieving, the samples were assayed in duplicate for Cr_2O_3 and for nitrogen.

The determination of Cr_2O_3 was carried out as described by Schürch (*8*) except for minor changes, which were made to increase the sensitivity of the method and to allow the use of smaller samples. Semimicro determinations of nitrogen in feces and intestinal contents were made by the method of Henwood and Garey (*9*), using duplicate 20-mg samples of dry material.

The results of the digestibility studies based on fecal excretion of nitrogen are given in the first section of Table 1. The coefficients of digestibility of 77 for the raw and 82 for the heated meal ration are similar to those reported by Melnick *et al.* (*6*) for raw and properly heated meals fed to rats.

[2] Fiducial limits at 0.01 level.

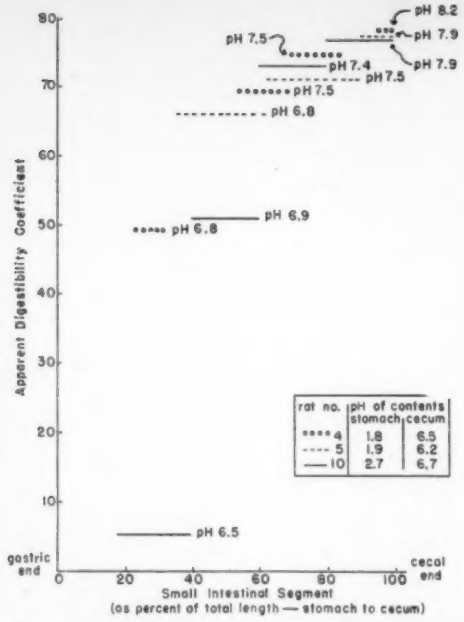

FIG. 1. pH and apparent nitrogen absorption in the small intestine of rats fed heated soybean meal.

The procedure for the study of rates of absorption of soybean nitrogen from the small intestine was as follows. Adult rats were fasted for periods of 24–36 hr. When several such fasted animals were killed (chloroform), the digestive tract was found to be empty except for cecal contents. After fasting, animals were fed the test rations for a period of at least 7 hr. They were then killed, and the digestive tract from esophagus to rectum was removed, freed from mesenteric attachments, and rinsed in cold tap water to remove blood. The small intestine was measured from stomach to cecum and cut into segments of known length and position. These segments were slit open, and the contents carefully removed from the mucosa. Animals were killed individually, and the above operations were carried out as rapidly as possible.

The contents of intestinal segments were placed on watch glasses, and their pH was determined, using a glass-calomel electrode system. They were then placed in a vacuum desiccator to be dried sufficiently for grinding. This required about 3 hr with a high vacuum pump. The dried samples were finely ground in an agate mortar to allow uniform sampling for Cr_2O_3 and nitrogen determinations.

The results of preliminary tests on rats fed the heated soybean ration indicated that with these animals near-maximum coefficients of digestibility for nitrogen were obtained with the contents of any segment of the terminal 40% of small intestine (Fig. 1). Contents of successive segments of small intestine of rats fed raw meal showed, in general, a progressive rise from an initial negative value but much lower apparent digestibility coefficients[3] throughout and greater variability.

These preliminary tests indicated that the use of only the terminal 20% of the small intestine would be satisfactory for a comparison of the two soybean rations. Only this segment was opened when the two rations were compared using larger numbers of animals. The same feeding technique and experimental procedure outlined above were employed. Results of these tests are given in the second section of Table 1.

These data indicate that, in rats fed raw meal ration, much of the nitrogen that escapes absorption in the small intestine must later be absorbed from the cecum or colon, since the coefficient of gross digestibility for the nitrogen of this ration is much larger than that estimated from the contents of terminal small intestinal segments. The greater variability of observed small intestinal coefficients of digestibility for animals fed raw meal ration is striking. An analysis of variance showed this difference between raw and heated meal rations to be highly significant.

A comparison of rat growth data with digestibility data suggests that the coefficient of digestibility estimated from the contents of the terminal portion of the small intestine may be closely related to utilization of nitrogen for growth. The grams gain in body weight per gram of nitrogen intake were 6.2 and 13.7 for the raw and the heated meal rations, respectively. Grams gain in body weight per gram of nitrogen absorbed from the small intestine[4] are 19 and 17 for the raw and the heated samples, respectively. Apparently the amino acids (or their nitrogen-containing derivatives) absorbed from the large intestine have little utility for growth, presumably as a result of bacterial activity.

The pH values for intestinal contents of rats of the two groups were similar. The mean values (terminal 20% of small intestine) were 7.82 ± 0.08[5] for rats fed raw meal ration, and 7.88 ± 0.09 for rats fed heated meal ration. The pH values of cecum contents were more variable and also were not significantly different for animals of the two groups. Mean values were 6.2 ± 0.4 and 6.5 ± 0.6 for animals fed raw and heated samples, respectively. It seems unlikely that significant "tryptic" hydrolysis could continue in the cecum under such conditions of pH, even though proteolytic enzymes may enter from the small intestine with escaping raw meal protein.

It seems possible that when raw meal protein escapes hydrolysis in the small intestine, substantial quantities of pancreatic or intestinal glandular secre-

[3] These coefficients of "digestibility" might better be termed coefficients of "net absorption," since in reality they represent the net absorption of nitrogen from the alimentary tract, rather than the total absorption of food nitrogen, as percentage of the nitrogen intake. Thus a negative coefficient is observed when nitrogen secretion overbalances nitrogen absorption.

[4] These calculations are based on the assumption that our digestibility data, obtained with adult animals, are applicable to the young animals used for growth tests.

[5] Fiducial limits at 0.05 level.

tions may be lost with it into the large intestine. This is suggested by our observation of several "negative" coefficients. Kunitz (*10*) has reported a stoichiometric, undissociable compound formed by combination of trypsin-inhibitor with trypsin. If significant amounts of secreted proteins are lost in this way, the "methionine-rich" complex observed by Bouthilet *et al.* (*11*) in the feces of chicks fed raw meal could be of endogenous origin. If such lost endogenous protein is high in methionine (relative to soybean protein), the degree of methionine deficiency of animals fed raw meal would be more severe than that estimated by consideration of the amino acid composition of soybeans. Such a sustained loss of secretions may be related to the pancreatic hypertrophy and increased concentrations of trypsinogen and chymotrypsinogen in pancreatic tissue reported in animals fed raw soybeans (*12*).

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Tissue Hemolysins

Olive McElroy, William Jordan, and Monroe E. Freeman

Department of Biochemistry, Army Medical Service Graduate School, Washington, D. C.

Among the many reports on tissue hemolysin published during the past fifty years, cis-vaccenic acid (*1, 2*) has been the only nonspecific hemolysin isolated from tissue extracts and clearly identified. However, the conclusion by Laser (*3*) that there seems to be no need for further speculation regarding their nature appears hardly acceptable in view of the evidence for the hemolysins found in incubated tissue. Laser's procedure for the extraction of the unsaturated acid from horse brain did not clearly indicate any incubation period or definite opportunity for enzymatic activity, thus suggesting the presence of free cis-vaccenic acid or an unstable complex easily broken by the chemical procedure.

If attention is focused on pathological states, it seems relatively unimportant whether hemolysins exist free in normal healthy tissue or whether they are potentially present as enzyme-substrate-inhibitor systems, capable of producing active hemolysin when disturbed by tissue injury or disease. This has led many previous workers to examine diseased tissue, when available, or more often normal tissue, minced, extracted, and incubated sufficiently to produce substantial amounts of active hemolysin. Such treatment has frequently demonstrated (*4–8*) (*a*) that the hemolysins do not arise from contaminating microorganisms; (*b*) that heat, prior to incubation, prevented the development of hemolysins in tissue extracts; (*c*) that a few hours of incubation greatly increased the hemolytic activity; and (*d*) that the active lysin could usually be extracted with alcohol or ether.

TABLE 1

Hemolytic Activity of Tissue Hemolysin and Oleic Acid

Mg fatty acid*	Time of complete hemolysis (min)	
	Tissue hemolysin	Oleic acid
0.22	1.5	3.0
.18	3.0	4.5
.09	12.5	40.0
0.07	51.0	> 90.0

* Fatty acid dissolved in 8 ml phosphate buffer, pH 7.3, 2 ml 2% suspension sheep erythrocyte added to each tube.

Experiments in this laboratory have shown that if storage or incubation (4°–37° C), hot solvents, and strong alkaline or acid reagents were avoided, fresh liver, kidney, and testes of rabbit, guinea pig, rat, and cattle yielded no more than traces of hemolytic materials. On the other hand, after a few hours' incubation at 37° C, a strongly hemolytic material could be extracted with cold alcohol.

Current experiments have led to the isolation of a very active hemolysin from incubated saline extracts of bovine testicular tissue. This purified material proved to be a highly unsaturated acid not identical with the octadec-11-enoic acid identified by Morton *et al.* (*2*) in horse brain extracts. It is present in no more than traces in normal healthy tissue, but is readily obtained in the following manner.

Bovine testes were ground, extracted with 0.9% saline, and centrifuged. The supernatant material was titrated to pH 4.5 with acetic acid and centrifuged. The precipitate was suspended in saline at pH 6.2, incubated 8–12 hr at room temperature (20° C), and extracted with ethanol. The active hemolysin in the ethanol extracts was separated from inactive lipoid materials by an extensive series of transfers (detailed elsewhere) between organic solvents and aqueous solutions, at acid, neutral, and alkaline pH. A short bath, low temperature, and low pressure distillation finally yielded a light yellow oil with a molecular weight of 310 + 10 and an iodine number of 257 (Hanus).

Table 1 shows the action of the tissue hemolytic acid in comparison with oleic acid. Hemolysis was inhibited by lecithin but not by cholesterol.

When the precipitate obtained at pH 4.5 was heated at 100° C prior to incubation, no hemolytic

material could be extracted by the process used. When the isolation procedure was carried out rapidly at −2° C, no active hemolysin was found. These ethanol extracts were evaporated under reduced pressure, taken up in ether and precipitated in acetone. This inactive acetone soluble fraction was suspended in phosphate buffer at pH 7.0 and incubated for 2 hr at 37° C with an inactive saline extract of acetone-dried tissue. The incubation mixture of the two inactive fractions yielded an active hemolysin that could be extracted in the manner described above.

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Inactivation of Vaccine Virus by Preparations of Hyaluronic Acid with or without Hyaluronidase: Experiments on Cell Cultures[1]

F. and M. L. Duran-Reynals[2]

Department of Microbiology,
Yale University School of Medicine,
New Haven, Connecticut

The purpose of this preliminary note is to report on the effects of preparations rich in hyaluronic acid, with or without the addition of hyaluronidase, on vaccine virus grown in media of the Maitland type. The materials were added to the cell-containing media, together with the virus, in an attempt to imitate the ground substance of the mesenchyme and thus duplicate, more or less remotely, the conditions that one can imagine prevail during infection (*1*).

We worked with 14 different preparations of either hyaluronic acid or potassium hyaluronate, often highly purified, made from either human umbilical cord or cattle vitreous humor.[3] Saline solutions of these materials were employed (*a*) fresh, after filtration through Berkefeld N candles, (*b*) steamed for 15 min, and (*c*) autoclaved at 120° for 15 min; and at each passage they were added to the cultures, containing 10 ml of medium, generally at the amount of 1 ml of a 1% solution, so that a final concentration of 1:1100 resulted. All the preparations, whether or not they had an inactivating effect on the virus, had a pH ranging from 4.0 to 5.0. Upon addition to the medium the pH of the latter dropped to around 6.8, with some preparations, to return to its normal of 7.2–7.5 shortly after, and remaining so until the end of the culture growth 5 days later. The hyaluronidase preparation[4] was used at a 1% dilution in saline after filtration through Berkefeld N candles. About 200 different lines of cultures, mostly with the Levaditi and dermal strains,[5] were obtained, each line consisting of 1–30 passages. The cultures were titrated on rabbits by intradermal inoculation of progressive tenfold dilutions of the supernatant fluid.

The significant results obtained ranged from a slight decrease in the virus titer to its complete inactivation. This variation on the effects of the polysaccharide preparation depended on the following factors:

a) Source of the preparation: preparations from cattle vitreous humor had less inactivating power than those from human umbilical cord.

b) Concentration of the solution: the inactivating effect was in direct relation to the strength of the solution.

c) Simultaneous addition of hyaluronidase: all preparations that failed to inactivate the virus did so upon addition of hyaluronidase.

d) The culture material employed, whether supernatant fluid or cells, in carrying the passage: the cells afforded extreme protection to the virus.

e) Strain of virus used: dermo vaccine was far more resistant than the Levaditi neuro vaccine.

The order of the neutralizing effect was as follows: Vitreous humor preparations at a final concentration of 1:1100, whether fresh, steamed, or autoclaved, had no effect on the dermo virus other than to reduce the average titer by approximately a one-tenth dilution below the control, whereas the 3 preparations inactivated the neuro vaccine in 3–6 passages. All preparations of umbilical cord at a final concentration of 1:1100 inactivated both strains of virus in 1–5 passages.

Steamed hyaluronic preparations from vitreous humor used at a final concentration of 1:600 completely inactivated the neuro virus, usually in one passage and caused a reduction of two-tenths dilution in the titer of the dermo virus. On the other hand, preparations from both vitreous humor and umbilical cord at final concentrations of 1:10,000 and 1:100,000 did not affect virus growth, or affected it very little.

When the hyaluronic acid preparations inactive at a concentration of 1:1200 were added to the cultures together with the hyaluronidase preparation, also at the final concentration of 1:1200, the virus was totally inactivated after 1–3 passages. The phenomenon is all the more remarkable if one considers that free hyalu-

[1] This investigation was supported by a grant from the Division of Research Grants and Fellowships, U. S. Public Health Service.

[2] With the collaboration of Phyllis Johnson.

[3] Seven of the preparations, supplied by the Wyeth Institute of Applied Biochemistry of Philadelphia, were prepared by H. E. Alburn and E. C. Williams (*2*); another five were prepared and supplied by Z. Hadidian (*3*) from the Tufts Medical School of Boston, and the other two were obtained in our laboratory by R. H. Pearce.

[4] Supplied by J. Seifter, of the Wyeth Institute of Applied Biochemistry. The enzyme contained 1,000 TRU/mg.

[5] The dermo virus, secured through F. L. Horsfall, was the strain cultured by Rivers and Ward (*4*) in 1933 and kept lyophilized since.

ronidase is still present in the cultures when tested on rabbit skin, and the resulting spreading of any virus left in the inoculum should lead to enhanced lesions.

In all the cases where total inactivation of the virus was obtained the effect was noticeable from the first or second passage by progressive reduction of titer and of size of the lesions till complete suppression. It is important to point out that we have occasionally obtained unpredictable results with some of the steamed preparations of hyaluronic acid. These preparations inactivated the virus in some experiments but failed to do so in others, the same happening when hyaluronidase was added. An effort is being made to elucidate the cause of the phenomenon, keeping in mind the possibility that steaming might affect the hyaluronic acid in such a way as to permit the development of resistant variants; in one instance, at least, we suspect this to be the case.

When passing the cultures by cells, we obtained only complete inactivation of the neuro vaccine with autoclaved preparations from umbilical cord in 2 out of 3 cases. All the other preparations, with or without hyaluronidase, were ineffective, in the course of perhaps 20 passages, except for a decrease in titer of 1–2 tenfold dilutions below the control.[6]

The protection thus afforded the virus by the cell seems to indicate that the effect of the polysaccharide preparation is directly on the virus and not on the cells, resulting in interference with the process of virus multiplication. To investigate this point further the hyaluronic acid preparation was added to the media from 30 min to 24 hr before or after being seeded with the virus, with no differences in the results. Still another test was to inject intradermally in the rabbit the washed cells of cultures the supernatant fluid of which, undiluted, had become inactive through the effect of the hyaluronic acid preparation: vaccinial lesions were obtained of about the same size and severity as those induced by the cells of control cultures.

Several of the conditions in our experiments and phenomena observed therein duplicate what takes place during infection of the animal. First of all, the concentration of hyaluronic acid, at about 1:1000, was not above what can be roughly assumed is present in the ground substance of several tissues, even disregarding a probable increase of the polysaccharide during inflammation. Further, it is well known that the hyaluronic acid of this ground substance is depolymerized and hydrolyzed by hyaluronidase as well as by other means, and it is this specific enzyme that, attacking its substrate in our cultures, brought to a maximum the inactivating effect of hyaluronic acid on vaccinia. Finally, the generally recognized fact in animal infection of the protection against injurious agents afforded to viruses by cells was also clearly observed in our tests regarding the effects of the hyaluronic acid preparations.

This investigation should obviously be expanded before what is above suggested becomes a conclusion, but if the results obtained so far do in any way duplicate what happens in the organism during infection it could be assumed that hyaluronic acid, and conceivably other polysaccharides, of the ground substance, especially after its degradation during infection, act to inactivate vaccinia and other infectious agents.[7] If this were so the ground substance besides being a *mechanical* barrier (*1*) would also be a *sterilizing* barrier to the progress of infection.

[6] The cell passages were carried out by transfer of most of the sediment obtained by light centrifugation of the cultures, so that in the successive passages cells progressively accumulated in amounts high above those generally employed in virus cultures. Incidentally, this method of cell passage has resulted in the practically indefinite maintenance of ordinary cultures, which, if passed by transfer of the supernatant fluid, would soon have been lost.

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Reversal of the Diabetogenic Action of Alloxan by Sulfhydryl Compounds

Parimal Bikash Sen and Gangagobinda Bhattacharya[1]

Department of Physiology, University College of Science and Technology, Calcutta, India

Large doses of sulfhydryl compounds, given prior to intravenous diabetogenic doses of alloxan, prevented diabetes in rats (*1, 2*). Prevention failed to occur, however, when the sulfhydryl compounds were given 5 min after the alloxan. Thus the action of alloxan could not be reversed.

The fundamental action of alloxan is completed within a few minutes after it reaches the blood, the necrosis of the β-cells of the islets of Langerhans being the ultimate result of this initial action (*3*). Attempts to reverse the action of alloxan should therefore be made after the completion of the action but before the onset of β-cell degeneration. The action of alloxan carried to its final stage of cell necrosis is not likely to be reversed. In rats changes in the β-cells only become evident microscopically 24 hr after intraperitoneal injection of alloxan as contrasted to their early appearance (5 min to 1 hr after injection) when alloxan is given intravenously (*4*). This suggested reinvestigation of the problem after intraperitoneal or subcutaneous administration of alloxan. The subcutaneous route was preferred, as it produced diabetes more consistently. A 175 mg/kg dose of alloxan produced diabetes in 100% of young rats

[1] Lady Tata Memorial Research Scholar.

previously fasted for 24 hr. This dose was used throughout the experiments. BAL and cysteine were the sulfhydryl compounds used.

Young rats, each weighing about 100 g and previously fasted for 24 hr, were subcutaneously injected with 175 mg/kg dose of alloxan. Solution of BAL in arachis oil (Boots) was then given to the rats intramuscularly at varying intervals. The presence of sugar in the urine for 2 consecutive days and a blood sugar value over 160 mg% for a similar period of time were considered to indicate a diabetic condition. The results are given in Table 1.

TABLE 1

EFFECT OF INTRAMUSCULAR INJECTION OF BAL ON PREVENTION OF DIABETES PRODUCED BY SUBCUTANEOUSLY INJECTED ALLOXAN IN 175 MG/KG DOSE*

No. rats used	Interval between administration of: Alloxan and first dose of BAL (75 mg/kg)	First and second doses of BAL (50 mg/kg)	Second and third doses of BAL (50 mg/kg)	Diabetic rats (%)
5	10 min	Not injected	Not injected	100
6	10 "	2–3 hr	" "	30
6	10 "	1 hr	1 hr	0
5	15 "	Not injected	Not injected	100
8	15 "	2–3 hr	" "	75
6	15 "	1 hr	1 hr	0
3	30 "	2–3 hr	Not injected	100
6	30 "	1 hr	1 hr	50
10	30 "	½ "	1 "	20
3	60 "	1 "	1 "	100
6	60 "	½ "	1 "	100

* BAL was given after the alloxan.

In the course of the above studies the effect of the administration of BAL before the alloxan was also studied. A 75 mg/kg dose of BAL when given 15 min before alloxan offered complete protection from diabetes. The same dose of BAL when given 10 min after alloxan could not, however, prevent diabetes (Table 1). Thus the fundamental action of the subcutaneous dose of alloxan was completed within this period of time. Repeated administration of BAL, however, offered considerable protection even when the treatment with BAL was started as late as 30 min after alloxan. Pancreas of rats in which diabetes had been completely prevented by BAL showed normal islet tissue. Thus the prevention of diabetes was essentially due to a reversal of the fundamental action of alloxan.

In the above-described experiments maximum protection was obtained with a 175 mg/kg total dose of BAL given in divided doses—a first dose of 75 mg/kg, followed by a second dose of 50 mg/kg ½ hr later and a third similar dose after another hour. These experiments were repeated with cysteine-HCl, which

TABLE 2

EFFECT OF REPEATED ADMINISTRATION OF CYSTEINE-HCl ON PREVENTION OF DIABETES PRODUCED BY SUBCUTANEOUSLY INJECTED ALLOXAN IN 175 MG/KG DOSE*

No. rats used	Interval between the administration of: Alloxan and first dose of cysteine-HCl (200 mg/kg)	First and second doses of cysteine-HCl (125 mg/kg)	Second and third doses of cysteine-HCl (125 mg/kg)	Diabetic rats (%)
10	30 min	30 min	1 hr	30
3	60 "	30 "	1 "	100

* Cysteine-HCl was given subcutaneously after the alloxan.

was given subcutaneously in aqueous solution without prior neutralization. A total of 450 mg/kg dose of cysteine-HCl approximately equivalent in its SH content to a 175 mg/kg dose of BAL was administered in proportionately divided doses and at the same rate as BAL. The first dose of cysteine was given only 30 and 60 min after alloxan. Earlier administration of cysteine was considered unnecessary. The results given in Table 2 show that repeated administration of cysteine also offered protection from diabetes and that the degree of protection was practically the same as with the corresponding dose of BAL.

The effect of the total 175 mg/kg dose of BAL given in a single injection after alloxan could not be studied because of the lethal effect of such a single dose on rats. The corresponding 450 mg/kg dose of cysteine-HCl was found to offer no protection when given in a single injection as early as 10 min after alloxan. This, together with the general sequence of the results obtained, shows that maintenance of a high concentration of the sulfhydryl compounds in the blood for a fairly long period of time was essential for the reversal of the action of alloxan.

Inhibition of essential sulfhydryl enzymes of the β-cells has been suggested as the mechanism of the diabetogenic action of alloxan (*1*). The reversal of the action of alloxan by BAL and cysteine reported here adds considerable strength to this view. The mechanism of the inhibition of the enzymes, however, seems to consist of oxidation of the essential SH groups to the —S—S— stage and not of formation of addition compounds between alloxan and the enzymes, as has been suggested by Lazarow and his co-workers (*2, 5*). Had the latter hypothesis been true, cysteine, which does not form an addition compound with alloxan (*5*), would be incapable of reversing its action. Both BAL and cysteine could not prevent diabetes when given 1 hr after alloxan. The inhibition of the enzymes was probably carried to an irreversible stage after this period of time. This may be due either to a further oxidation of the SH groups beyond the —S—S— stage, or to the onset of subsidiary irre-

versible changes in the enzymes. In neither case would the added sulfhydryl compounds have any reactivating effect.

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Enzymatic Hydrolysis of Dextran

Virginia Whiteside-Carlson and
Warner W. Carlson

Department of Biochemistry and School of Dentistry, Medical College of Alabama, Birmingham

The preparation of blood volume extenders from dextran currently is based on partial acid hydrolysis of the bacterial polysaccharide, with subsequent solvent fractionation of the hydrolysate to yield products with average molecular weights approximating those of plasma albumins (*1, 2*). Ingelman (*3*) and Nordström and Hultin (*4*) have reported the presence of enzymes capable of hydrolyzing dextran in filtrates from cultures of *Cellvibrio fulva, Penicillium lilacinum, P. funiculosum,* and *Verticillium coccorum.* The main effect of these enzymes on the polysaccharide is the production of reducing sugars, with the result that they have been of no practical value in the preparation of partially degraded dextrans.

For the past year we have been inoculating dextran-salts solutions with various soil samples, and also allowing such solutions to be exposed to airborne contaminants, in an attempt to isolate organisms capable of attacking dextran. Among a number of such isolates we obtained an *Aspergillus* sp. which has proved useful for the purpose of degrading various dextrans. Filtrates from cultures of the mold in media containing dextran are highly active in splitting the polysaccharide. Only a small amount of reducing sugar is produced during the time required for the filtrates to degrade the polysaccharide into fragments with an average molecular weight in the region of 75,000. By analogy with the α-amylases (*5*), the enzyme formed by this mold probably should be termed an endo-dextranase, since it appears to have a preference for splitting glucosidic linkages remote from end groups. We have found the enzyme to be active against dextrans obtained from 4 different strains of *Leuconostoc.* Active concentrates of the enzyme have been prepared by fractional precipitation of mold filtrates with ammonium sulfate.

A particular advantage of this method of hydrolysis is that the enzyme solution can be allowed to act directly on fermented culture media containing dextran. This eliminates the preliminary precipitation of the polysaccharide with alcohol, as called for in the scheme employing acid hydrolysis (*1*). Since the enzymatic hydrolysis proceeds at room temperature, it is easy to obtain partially hydrolyzed dextrans free from objectionable color.

A typical experiment was carried out as follows: Eight liters of a 20% sucrose medium was fermented with *Leuconostoc mesenteroides* 683, yielding a solution containing dextran in a concentration of 6.1%. Eighty ml of the mold filtrate was added, and enzymatic action allowed to proceed for 40 min, during which time the viscosity of the solution decreased rapidly. The action of the enzyme was stopped by adding alkali to pH 9. The solution was then fractionated with alcohol in the usual manner (*1*), yielding 400 *g* of a white product with an average molecular weight of 71,000, as determined by viscometry (*6*).

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Blocking of Action of Acetylcholine by Barbiturates

Henry E. Fernando[1]

Department of Entomology, University of Illinois, Urbana

The barbiturates have proved to be an important group of depressants of the central nervous system since their introduction for clinical trial in 1912 on the basis of the studies of Loewe (*1*), Juliusburger (*2*), and Impens (*3*). In anesthetic doses all the barbiturates inhibit convulsions such as occur in strychnine poisoning, tetanus, and epilepsy. Notwithstanding their continuous use in chemotherapy since their introduction in 1912, evidence of their mode of action has been scanty. Thus Schütz (*4–6*) has shown that there is a progressive decline of cholinesterase activity of human serum and in guinea pig serum, muscle, and certain nervous tissues, during prolonged treatment with a barbiturate. Heinbecker and Bartley (*7*) have shown in their studies with peripheral nerves that phenobarbital increases threshold and at the same time prolongs recovery time of neurones after impulse propagation. Eccles (*8*) showed that phenobarbital blocked two-neurone transmission in the spinal cord primarily by increasing the extent of local depolarization required for initiation of a propagated impulse by motoneurone soma. The author's interest in the

[1] The author wishes to acknowledge his indebtedness to C. L. Prosser, of the Department of Physiology, University of Illinois, Urbana, and J. H. Welsh, of the Harvard University Biological Laboratories, Cambridge, Mass., for their valuable suggestions on techniques in the use of Venus heart.

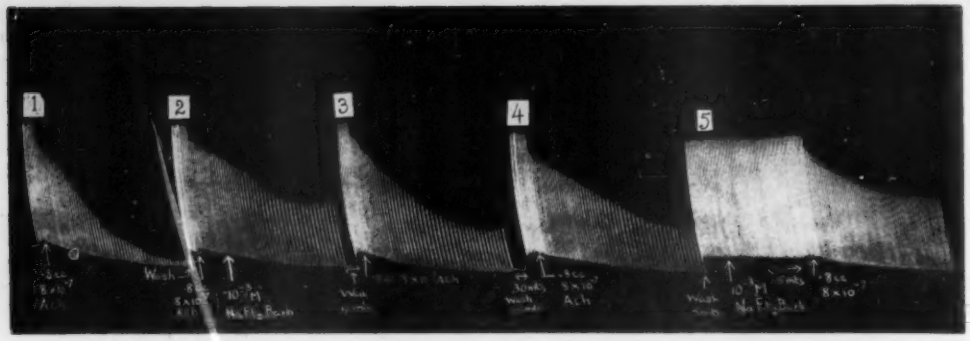

FIG. 1. Record of Venus heart showing blocking of acetylcholine by sodium diethyl barbiturate (Test 1).

barbiturates arose from the fact that these compounds are important antidotes for poisoning of both insects and mammalian subjects by the chlorinated hydrocarbon insecticides. Thus, Bodenstein (*9*) showed that symptoms of DDT poisoning (hyperactivity, tremors, convulsions) in flies (*Drosophila*) could be prevented by injection of 1% phenobarbital, whereas his reciprocal experiments demonstrated that pretreatment of flies by injection of 1% phenobarbital followed by DDT prevents the appearance of symptoms of DDT poisoning. Furthermore, phenobarbital is the only antidote recommended by the U. S. Public Health Service (*10*) for poisoning of humans and domestic animals by dieldrin, one of the chlorinated hydrocarbon insecticides. Therefore, in the course of investigations involving the changes in levels of acetylcholine-like substances in the central and peripheral nervous system of the American roach *Periplaneta americana* (L.), during poisoning by these insecticides, the author felt it might be of value to investigate the action of barbiturates on the activity of acetylcholine.

Hearts of the pelecypod mollusk *Venus mercenaria*, employed earlier for several hours of bioassay of Ach (acetylcholine)-like substances in insect nervous tissue, were used to study the action of barbiturates on the activity of Ach. The high sensitivity of this preparation to Ach was first described by Prosser (*11*), and techniques for its use in bioassay of Ach have been described by Wait (*12*) and Welsh and Taub (*13*). Sea water at 15°–18° C was the fluid used in the bath. A standard solution of Ach was prepared in a 5% solution of sodium dihydrogen phosphate, and concentrations required for tests were prepared immediately before use by dilution of aliquots in sea water. Barbiturates used in this study were the sodium salts of 5, 5-diethyl barbituric acid and 5, 5-phenyl ethyl barbituric acid. Required concentrations of the barbiturates were prepared in sea water before use. Test solutions were introduced at the bottom of the heart bath by way of a 2-ml hypodermic syringe with its needle bent at right angles. The concentrations of Ach represented on all the plates indicate the amount of Ach in g/ml added to the 20-ml heart bath, and those of the barbiturates indicate the final molar concentrations in the 20-ml bath.

Concentrations of 10^{-4} *M* sodium diethyl barbiturate had little or no effect in blocking the action of Ach on

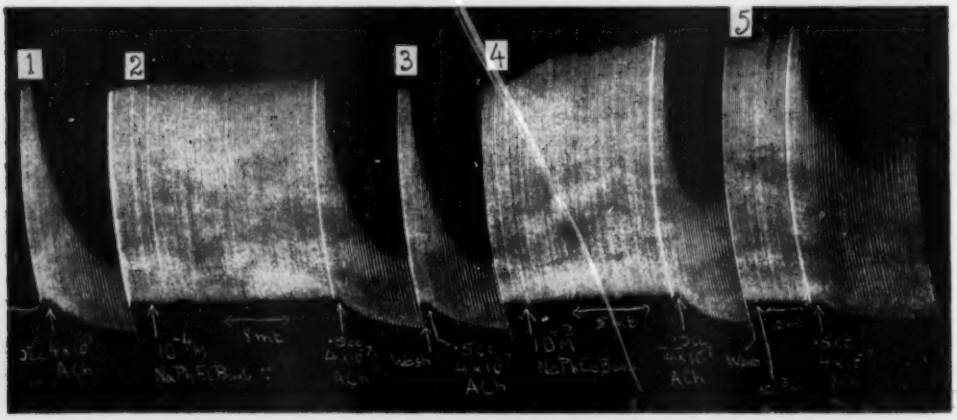

FIG. 2. Record of Venus heart showing blocking of acetylcholine by sodium phenobarbital (Test 2).

the heart. Records of tests with 10^{-3} *M* sodium diethyl barbiturate are shown in Fig. 1. In Test 1, the addition of .8 ml 8×10^{-7} Ach into the heart bath is shown to result in a 95% inhibition of the amplitude of heartbeat. In Test 2, after washing and complete recovery of the heart, .8 ml 8×10^{-7} Ach was added to the bath, followed during inhibition of beat by treatment of the heart with 10^{-3} *M* sodium diethyl barbiturate. Inhibition of the amplitude of the heartbeat was now only 50%, 10^{-3} *M* sodium diethyl barbiturate having blocked 45% of the action of the Ach. Tests 3 and 4 were designed to discover whether the Ach-blocking action of the barbiturate could be washed away, and, if this was not so, how long it lasted. These tests show that a time lapse of 40 min involving about 20 min of washing after barbiturate treatment resulted in only a small reduction of the Ach-blocking action. This makes apparent immediately the impracticability of attempting to compare the action of two or more barbiturates on the same heart. In Test 5, the heart was pretreated for 5 min with 10^{-3} *M* sodium diethyl barbiturate before addition of .8 ml 8×10^{-7} Ach. This treatment resulted in only a 37.5% inhibition of amplitude of heartbeat.

Fig. 2 shows the records of tests with sodium phenobarbital at concentrations of 10^{-4} *M* and 10^{-3} *M*. In Test 1, the addition of .5 ml 4×10^{-7} Ach is shown to result in 71.4% inhibition of amplitude of heartbeat. Test 2 indicates the effect of pretreatment of the heart for 8 min with 10^{-4} *M* sodium phenobarbital followed by the addition of .5 ml 4×10^{-7} Ach to the bath. This treatment resulted in a small blocking of the action of the Ach, for the percentage of inhibition was now 66.25. Test 3 would suggest that this low Ach-blocking action by 10^{-4} *M* sodium phenobarbital is washed away to some extent (percentage inhibition, 69.6). In Test 4, the heart was pretreated for 5 min with 10^{-3} *M* sodium phenobarbital, followed by the addition of .5 ml 4×10^{-7} Ach to the bath. Two results of treatment with phenobarbital are now apparent. First, there is a marked increase in the amplitude of heartbeat (18%), and, second, the action of Ach is blocked more significantly. The percentage of inhibition was 54.5. It was felt, however, that 5 min pretreatment of the heart with the barbiturate was not long enough. The heart was treated again for 2 min with 10^{-3} *M* sodium phenobarbital, and then .5 ml 4×10^{-7} Ach was added to the bath. This further pretreatment with the barbiturate resulted in a more marked blocking of the Ach, since a 42.8% inhibition of amplitude of heartbeat ensued.

Fig. 3 shows the effect of sodium phenobarbital in blocking Ach on a heart more sensitive to Ach than those used in the previous tests. In this series of tests a concentration of Ach was selected which was more than that required for 100% inhibition of the heartbeat. In Test 1, .5 ml 2×10^{-7} Ach is shown to cause complete inhibition of the heartbeat. Test 2 shows the effect of treatment of the heart with 10^{-3} *M* sodium phenobarbital after the heart started toward total inhibition by the addition of .5 ml 2×10^{-7} Ach. Complete inhibition of the heartbeat was prevented by this treatment, and it resulted in 91.6% inhibition of amplitude of beat. In Test 3, the heart, after washing and recovery, was pretreated with 10^{-3} *M* sodium phenobarbital for 5 min, followed by the addition of .5 ml 2×10^{-7} Ach to the bath. Here, again, sodium phenobarbital caused an increase in amplitude of heartbeat (33.3%). The percentage of inhibition of amplitude of heartbeat was only 25% under these conditions.

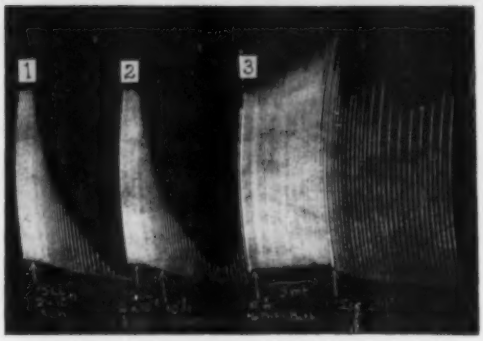

FIG. 3. Record of Venus heart showing blocking of acetylcholine by sodium phenobarbital (Test 3).

In all tests with the two barbiturates used in this investigation, the effect of blocking the action of Ach on the Venus heart was a consistent feature. However, with preparations that normally gave an inconsistent pattern of beat, the response to barbiturate treatment, like that to Ach treatment, was erratic. Although concentrations of 10^{-3} *M* barbiturate may be regarded as high for test purposes, it must be mentioned that the hearts used in these tests were of low sensitivity to Ach (usual threshold is reported to be between 10^{-10} and 10^{-11} g/ml Ach [*13*]). It may well be possible that with hearts of higher sensitivity to Ach the barbiturates would be effective Ach-blocking agents at concentrations of 10^{-4} *M* or 10^{-5} *M*, as is suggested by a comparison of the results shown in Figs. 2 and 3.

The results obtained here with the barbiturates used are very similar to those obtained by Welsh and Taub (*14*) when investigating the structure-activity relationships of Ach and quarternary ammonium ions. In this work it was found that quarternary ammonium ions with 3 or 4 alkyl groups other than methyl have an excitatory action on Venus heart and also reduce the effect of added Ach, just as sodium phenobarbital and sodium diethyl barbiturate were found to do in the present investigation. Holton and Ing (*15*) and Welsh and Taub (*14*) also found that at least 2 methyl groups are required for Ach-like activity of quarternary ammonium ions on the Venus heart. A study of the action of a large series of barbiturates on Venus heart might provide valuable information on the structure-activity relationships of these compounds and also serve to elucidate any relationship that may exist between these compounds and Ach.

As mentioned earlier, the finding of Schütz (*4–6*),

that prolonged barbiturate treatment results in a decrease of cholinesterase activity in serum and other tissues of mammalian subjects *in vivo*, has been confirmed in our *in vitro* studies with insect cholinesterase. Our studies on the changes in levels of the Ach-like substance in the insect nervous system during the course of poisoning by the chlorinated hydrocarbon insecticides show significant increases of this substance and also suggest a potentiation of the cholineacetylase system during such poisoning. Taking these facts into consideration, it may be suggested that the efficiency of the barbiturates as anticonvulsants depends, if not entirely, at least mainly, on their blocking of the action of Ach. The fact that withdrawal of barbiturate treatment may often give rise to *de novo* convulsions, may be the result, after metabolism of the barbiturate, of the partial destruction or inhibition of cholinesterase by the active barbiturate at its site or sites of action.

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Electron Microscopy of Human Erythrocytes from Healthy and Sludged Blood[1]

Edward H. Bloch[2] and Allen Powell

Department of Anatomy,
Western Reserve University, and
Case Institute of Technology, Cleveland, Ohio

Microscopic observation of the circulating blood of man, ill with a variety of disease processes, has shown that the red blood cells were struck into aggregates which varied in size and rigidity (*1–3*). In many diseases where tough red cell aggregates were seen *in vivo*, and coatings were presumed to hold these aggregates together, such coatings could not be demonstrated *in vitro* by light- or dark-field microscopy. Electron microscopy was undertaken to obtain better definition of the surface of the agglutinated red cells and thus to be able to demonstrate the morphology of the coatings.

The blood vessels of the human bulbar conjunctiva were obliquely illuminated, and a binocular biobjective microscope was focused on the circulating blood, which was studied at 48–150 diameters magnification (*4*). The results of the observations were recorded on a special chart.

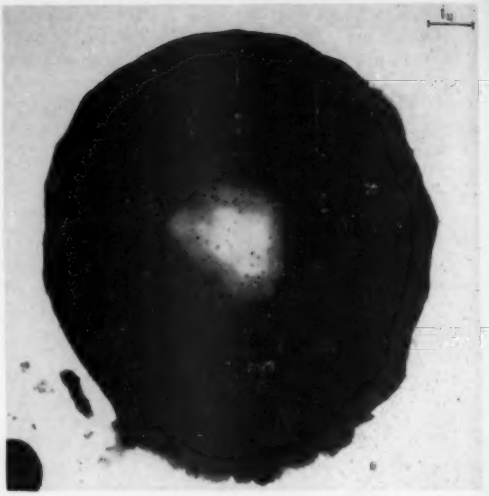

Fig. 1. Electron micrograph of a human red blood cell obtained from a healthy circulation. ×2000. Salt crystals are stuck to the lower border of the cell and can also be seen through center portion.

Two groups of subjects were used. In the first group were those who had a healthy circulation (*2*). This kind of circulation was demonstrated in clinically healthy subjects, as well as in those who were clinically ill but had a disease process which did not produce a sludge, or those who had had a pathologic circulation but had been treated and a normal circulation had been re-established. In the second group of patients were those who were clinically ill and had definite intravascular pathology characterized by the presence of a sludge which significantly reduced flow through arterioles. Such patients often had red cell aggregates with visible coatings.

Each patient's circulation was studied 24 hr before and immediately prior to the withdrawal of the blood for electron microscopy. The blood was obtained from the median cubital vein of the arm and was drawn directly into heparin, with the ratio of blood to heparin varying from 1:1 to 1:6. After withdrawal the blood and heparin were gently agitated in the syringe, and then 0.2–1.0 ml of the mixture was slowly ejected into 8–10 ml of mammalian Ringer's solution.

Electron microscopy of such blood was usually made within a period of 30–60 min after withdrawal. The diluted blood was prepared for electron microscopy by placing a small drop of the mixture upon a Parlodion film, which was placed on a 200-mesh screen. After 2 min the blood droplet was removed by absorption into filter paper, and the film with adhering red blood cells was air-dried and placed on the object holder. The

[1] This investigation was supported in part by a grant from the Life Insurance Fund.
[2] Established Investigator, American Heart Association.

preparations were studied on the viewing screen of an RCA microscope, and selected cells were photographed at magnifications ranging between 3,500 and 20,000 diameters.

Red blood cells from individuals having a healthy circulation were found by electron microscopy to have surfaces which had a sharp outline where no detail could be observed (Fig. 1). Such red blood cells were also found in small number in the blood of subjects who had sludged blood, where they were intermingled among the pathologic cells.

The blood obtained from patients who had sludged blood revealed red cells and/or red cell aggregates which had significantly altered surfaces. These red cells had a coating which covered the entire cell surface, was irregular in outline, varied in thickness, and was relatively amorphous in structure at magnifications up to 20,000 diameters (Fig. 2). Further, it was

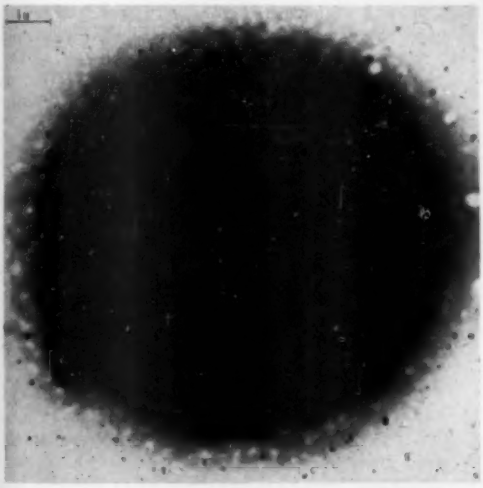

FIG. 2. Electron micrograph of a human red blood cell obtained from sludged blood (bronchopneumonia). × 2000. Note total increase in diameter of cell because of the coating, as compared with healthy cell of Fig. 1.

possible to obtain clumps of red cells and to demonstrate coatings not only covering the individual cells but also forming bridges between them (Fig. 3).

Since the demonstration, beginning in 1940, of sludged blood in human diseases, evidence has accumulated by various tests showing that the surfaces of the red cells of sludged blood are different from those of healthy blood. From direct microscopic observation of the living circulation came the evidence that the red cells of sludged blood were coated and were not infrequently bound together firmly by an appreciable amount of "new" substances of unknown composition. It was possible to demonstrate in the malaria of rhesus monkeys, *in vitro*, by dark-field microscopy, that the red cells of this sludge were held firmly together by a highly refractile substance. And it was possible to microdissect this coating and draw it into long, highly refractile, viscous filaments (*5*).

Although in the human diseases it has not hitherto been possible to demonstrate *in vitro* coatings on the

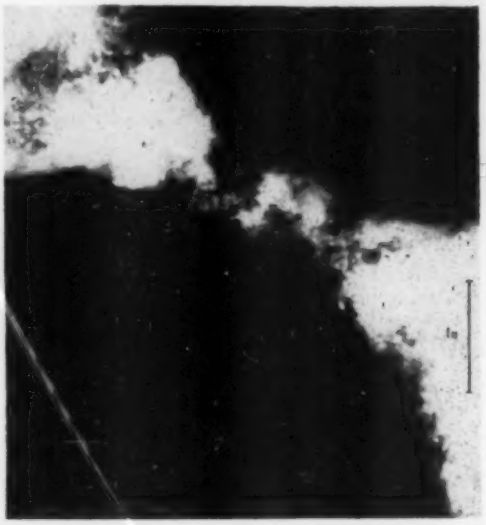

FIG. 3. Electron micrograph showing coating between two human red cells from sludged blood. × 5625.

red cells of sludged blood, it has been repeatedly demonstrated that the electrokinetic properties of these cells differed from the red cells of healthy blood (*6, 7*).

The demonstration of a coating on human red cells and aggregates by electron microscopy of sludged blood and of the absence of such coatings on the similarly treated red cells from healthy blood is in accord with and further buttresses the existing data that a marked change occurs on the surface of red cells in some diseases. Electron microscopy has not only given the first *in vitro* evidence of a coating on the human red cells from sludged blood but has also permitted a study of the coating's morphology.

Whether such coatings are derived principally from the cell or plasma still remains unanswered. Work is now in progress to characterize further the physical and chemical properties of the coatings on the red cells in human diseases.

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Comments and Communications

The Occurrence of *Branchiostoma* (*Amphioxus*) in Mississippi and Louisiana

On July 5, 1951, one of us (HMH), and R. L. Caylor, first found *Branchiostoma* while collecting just below low tide on the tip of Chandeleur Island, La., approximately half a mile from the lighthouse. Subsequent collecting has revealed its presence at the following locations on the outlying islands in Mississippi: Petit Bois Island, Aug. 7, 1951, found by Shoemaker and Caylor; Horn Island, Aug. 16, 1951, found by Caylor, Hefley, and Shoemaker; Ship Island, Aug. 21, 1951, found by Hefley and students of invertebrate zoology at the Gulf Coast Research Laboratory, Ocean Springs.

The specimens occur just below low tide line, usually in 2–4 ft of water, on clean sand bottom. Many were found associated with submerged marine vegetation; others were obtained in open sand.

The animals seem to be structurally quite close to *Branchiostoma caribaeum* Sundeval, 1893, with a few minor differences. In certain respects they resemble *B. bermudae* Hubbs, 1922, but have more myotomes (60 as compared with not more than 57 for *bermudae*). Preliminary counts show the fin rays to fall between 297 and 312, which lies within the range for *B. caribaeum* (227–330). Work on the exact determination of the form is proceeding.

This is the first account of the genus *Branchiostoma* occurring in the islands of Louisiana and Mississippi, and constitutes two state records for the genus.

Harold M. Hefley

Mississippi Southern College

Hurst Shoemaker

University of Illinois, Urbana

ASTIA and GSIS

In a footnote on the first page of our paper "The Planning of Libraries for Military Research Establishments" (*1*), we described the government-sponsored Armed Services Technical Information Agency (ASTIA) as the successor to the unofficial Group for the Standardization of Information Services (GSIS). Shortly after the publication of the paper, we were informed that our definition of this relationship was not quite correct. We also learned that Robert Bray of the Navy Research Section of the Library of Congress had submitted a communication to Science (*2*) in which he pointed out our error.

Although we regret any erroneous impressions created by the footnote in question, we must acknowledge that Mr. Bray's explanation of the relationship of the unofficial GSIS to the official ASTIA is more accurate than our explanation only because his is more current. Our paper was submitted to Science in February 1951; we were notified of its acceptance in April 1951; and it was published in July 1951. During this six-month period drastic changes in the character of the relationship of the two bodies apparently occurred.

We deduced the relationship that we described in our paper from a statement in the published proceedings of the *Symposium on Standardization in Technical Information Services for Government Contractors* (*3*) held in New York on Jan. 29, 1951. The statement, made by Eugene Scott, chairman of the symposium, in answer to the question "What is the relation of GSIS to ASTIA?" was as follows: ". . . GSIS is a sort of stepchild of ASTIA, which we hope will be adopted when ASTIA grows of age."

From the foregoing statement, and from similar remarks made at public meetings by other members of the unofficial Group for the Standardization of Information Services, we assumed that this was a forerunner, which was eventually to be succeeded or absorbed by the Armed Services Technical Information Agency.

Saul Herner
M. K. Heatwole

Applied Physics Laboratory
The Johns Hopkins University
Silver Spring, Maryland

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Fungicidal Properties of Antihistaminics

In the July 6, 1951, issue of Science (**114**, 15), I read with great interest an account by Reiss and Caroline of "The Metabolism of *Blastomyces dermatitidis*, Antagonists to the Growth-inhibiting Effect of Trimeton Maleate." They reported that *B. dermatitidis* was partially inhibited with 0.0003 *M* trimeton maleate, and the growth of the fungus was completely suppressed at 0.15 *M* concentration. Experimental *B. dermatitidis* infection in mice did not respond to subcutaneous injections of 40 mg/kg trimeton maleate.

Previously I read in the June 23, 1950, issue of Science (**111**, 689) the account by Carson and Campbell of "The Inhibitory Effect of Three Antihistaminics on the Growth of Fungi Pathogenic for Man." They tested pyribenzamine, antistine, and di-phenylpyraline against cultures of *Trichophyton, Microsporon, Epidermophyton, Histoplasma, Blastomyces, Cryptococcus,* and *Candida,* and found that diphenyl-pyraline and pyribenzamine possess properties that are inhibitory to pathogenic fungi.

A year before the paper of Carson and Campbell was published, we carried on experiments on the fungicidal properties of eight antihistaminics; namely, trimeton maleate, chlor trimeton, thephorin, antistine,

benedryl, histadyl, neoantergan, and pyribenzamine. The following pathogenic fungi were routinely used in these tests: *B. dermatitidis, Coccidiodis immitis, Trichophyton rubrum, Candida albicans,* and *Cryptococcus neoformans.* All the antihistaminics tested exhibited fungicidal properties, but thephorin and benedryl were the most potent. We submitted the manuscript first to a bacteriological journal and then to a pharmacological journal, but the paper was not accepted by either journal because, it was contended, the findings did not sound scientific. Discouraged, we decided not to publish our findings.

Now that two papers have been published on the fungicidal properties of antihistaminics confirming our earlier findings, in the interests of science we wish to state that

1) All antihistaminic compounds possess inhibitory effect on fungi.

2) The editors of scientific journals and their consultants must not turn down or refuse to publish a paper simply because the findings do not comply with their trend of thinking. They should use a scientific approach, free of prejudice, in accepting or refusing a manuscript. Opinionated thinking stops or delays progress.

HARRY SENECA

College of Physicians and Surgeons
Columbia University

Book Reviews

Nerve Impulse. Transactions of the first conference, March 2–3, 1950, New York. David Nachmansohn, Ed. New York: Josiah Macy, Jr. Foundation, 1951. 159 pp. $3.00.

Because of the enormous number of papers presented at national scientific meetings many sections must meet simultaneously. Lack of time and organizational difficulties do not favor critical discussions. This condition, aggravated by inadequate space in some of our leading journals and perhaps by some arbitrariness in editorial policies, accounts for the fact that our scientific archives become more and more storehouses of facts without proper correlation and evaluation of the data. Under these circumstances the venture of the Macy Foundation, of bringing leading scientists together for an informal discussion of important problems, is a laudable undertaking.

Nerve Impulse inaugurates a new series and covers several important topics. Grundfest introduces "Potentialities and Limitations of Electrophysiology," and Quastel deals with the biochemical approach to the problem of nerve conduction. This problem is further elucidated from the viewpoint of comparative physiology by Prosser and in its histological aspect, particularly with regard to synaptic transmission, by Bodian. A report on ion exchange and permeability concludes the book. The discussion is carried on at a very high level, and many more problems than are indicated by the review titles are competently dealt with. Some improvement in procedure and presentation seems desirable, however. Particularly in the first section, the discussion is rather turbulent and jumps too much from one topic to another as a result of lack of guidance by the chairman. This must have been felt by the participants, since in the last section the discussion is omitted but "incorporated" in Steinbach's report. The reprinting of a competently guided discussion that would steer between these two extremes would appear to this reviewer most helpful. It is further suggested that the references might be handled uniformly throughout the book. In spite of these criticisms this is a publication rich in information and in ideas.

E. GELLHORN

Department of Physiology
University of Minnesota Medical School
Minneapolis

Physik und Chemie des Zellkernes. Protoplasma-Monographien, Band 20. Petr F. Milovidov. Berlin-Nikolassee: Naturwissenschaftlicher Verlag, 1949. 529 pp.

Although the publication date of Milovidov's monograph is 1949, the author informs us that he wrote it in 1938–39 and managed to make some changes up to 1943. Completed about the time when the present tide of interest in the physical and chemical behavior of the cell nucleus was just beginning to rise, it can hardly be expected to reflect those specific problems that are the occasion of such intense activity today. Prague could hardly have been the ideal place to look into the future of nuclear physiology during those years.

Biology being more of a cumulative science than some others, a thorough work such as this retains value and even timeliness without being up to date. Bandwagons change more rapidly than tunes. In the case of nuclear function, most of our current viewpoints are restatements in chemical, and therefore more precise, terms of ideas derived earlier from microscopic observation. Thus, the hypothesis supported by tracer experiments, that a major activity of the nucleus is the synthesis of ribonucleic acid for deployment in the cytoplasm, is the heir to the older "chromidia" hypothesis, based on numerous descriptions of the passage of basophilic particles from nucleus to cytoplasm. In Milovidov's work, such older hypotheses are discussed thoroughly and with reference to a great wealth of specific cases. Milovidov's monograph merits serious study by those who are

interested in the cytological background to the interplay of cytology and biochemistry.

This work is more valuable, of course, in those areas that have tended to be neglected in recent years. For example, more than 30 pages (including 15 pages of tables!) are devoted to summarizing the results of attempts to stain nuclei vitally. A really successful solution of this problem would be a great asset, and such a conscientious summary of past experience is invaluable. Similarly, workers on cell division will appreciate the 5 pages of tables detailing the duration of various mitotic phases in a wide variety of materials.

The weakest aspect of Milovidov's book is the treatment of its stated subject—the physics and chemistry of the nucleus. Three hundred-odd pages are devoted to physics, some 60 to chemistry. What is reflected is the dominant fashion of a period in which it was felt that special merit attached to the assignment of a numerical value to any physical property of a biological system, however irrelevant to biological problems, and the restatement of visual observations in the language of the colloid chemistry of the time. A more recent book on the same subject would probably reverse the relative emphasis on chemical and physical aspects, and it is wholesome to wonder how this would appear in the same perspective.

Unfortunately, this volume lacks what would be a most valuable bibliography, whose publication is promised as part two of the complete monograph.

DANIEL MAZIA

Department of Zoology
University of California, Berkeley

Reviewed in Brief

The Physical Basis of Life. J. D. Bernal. London: Routledge and Kegan Paul, 1951. 80 pp. 6s.

One point not often dealt with in works concerning the origins of life is that of the genesis of organic compounds, especially those with a complexity comparable to that of proteins. Professor Bernal starts his monograph by outlining this problem and then considers some possible mechanisms in a frankly speculative but stimulating fashion. The title may be misleading because this work, a Guthrie lecture, deals almost entirely with the origins and early organization of biological processes. The discussion might be divided into the following sections: Possible ultraviolet photosyntheses, the rise of an organic molecule population, the initiation of living processes, the development of photosynthetic life, and, finally, some remarks on the organization of cellular processes. Throughout, the discussion is admirably annotated by N. W. Pirie.

The Structure and Mechanical Properties of Metals. Bruce Chalmers. New York: Wiley, 1951. 132 pp. $3.50.

This brief monograph, the second in a series on the structure and mechanical properties of metals, published under authority of the Royal Aeronautical Society, deals first with the structure of pure metals, using evidence from x-rays as well as heat treatment and etch figures. It then discusses the structure of alloys, making ample use of equilibrium diagrams and a brief outline of problems as they are encountered in disordered alloys and in diffusion.

Age hardening is illustrated in aluminum copper and copper beryllium. A chapter on the effect of the distortion of structure, using modern ideas about dislocations and surface arrangements, is followed by material on heat treatment, and this, in turn, is followed by a chapter on structure determination. The monograph closes with a discussion of the mechanical properties and their dependence on structure. The text is nonmathematical throughout and should be useful for engineering students and practical engineers as an introduction to the modern concepts of structure and metallic properties.

Selective Toxicity with Special Reference to Chemotherapy. Adrien Albert. New York: Wiley; London: Methuen, 1951. 228 pp. $1.75.

Biologists generally should find this little book an extremely useful guide to the physiological action of a variety of organic compounds. In many ways the volume complements the recent monograph of Danielli because, where Danielli deals largely with the theoretical aspects of cell pharmacology, this book approaches such problems from a practical or experimental viewpoint. The subject matter differs from a pharmacological review in that it presents information from the fields of microbial, insect, plant, and animal physiology. The fact that the author is able to relate the problem of selective toxicity to so widely separated groups of living organisms is most commendable.

The monograph starts with a consideration of a definition of selective toxicity and the feasibility of such an action. The complexity of the subject matter is such that probably an empirical approach, such as that adopted, is best at the present time. The chapter dealing with the physiological effects of hydrocarbons and other nonreactive substances is perhaps least satisfactory, because it is here that theory can best be applied. Viewed as a whole, however, the work is a most satisfactory contribution.

Scientific Book Register

Radiations from Radioactive Substances. Reissue. Sir Ernest Rutherford, James Chadwick, and C. D. Ellis. New York: Cambridge Univ. Press, 1951. 588 pp. $11.00.

Totem and Taboo. Some Points of Agreement between the Mental Lives of Savages and Neurotics. Sigmund Freud; authorized trans. by James Strachey. New York: Norton, 1952. 172 pp. $3.00.

The Chemistry and Technology of Food and Food Products, Vol. III. Rev. 2nd ed. Morris B. Jacobs, Ed. New York–London: Interscience, 1951. Pp. 1,773–2,580. $15.00.

Fundamentals of Automatic Control. G. H. Farrington. New York: Wiley, 1951. 285 pp. $5.00.

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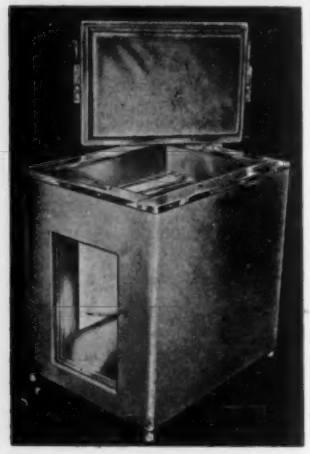

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Jan. 21–22. Compressed Gas Association (Annual). Waldorf-Astoria, New York.
Jan. 21–22. Josiah Macy, Jr. Foundation Conference on Blood Clotting. Cornell University, Ithaca, N. Y.
Jan. 21–25. American Institute of Electrical Engineers (Winter). Hotel Statler, New York.
Jan. 26. Metropolitan Detroit Science Club, Wayne University, and Institute for Economic Education. Institute and Industrial Exhibits on "Jobs Open to Science Trained High School Graduates." Wayne University, Detroit.
Jan. 28–31. Symposium on Modern Methods of Analytical Chemistry (Annual). Louisiana State University, Baton Rouge.
Jan. 29–31. American Meteorological Society. Roosevelt Hotel, New York.
Jan. 29–Feb. 2. American Library Association (Midwinter). Edgewater Beach Hotel, Chicago.
Jan. 31–Feb. 1. American Society for Metals (Midwinter Technical). William Penn Hotel, Pittsburgh.
Jan. 31–Feb. 2. American Physical Society (Annual). Columbia University, New York.
Feb. 1–2. Protein Conference (Annual). Bureau of Biological Research, Rutgers University, New Brunswick, N. J.
Feb. 3–8. American Society for Testing Materials. The Shoreham, Washington, D. C.
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Feb. 15–16. Mathematical Association of America (Louisiana-Mississippi Section). Northwestern State College, Natchitoches, La.
Feb. 17–24. Brotherhood Week.
Feb. 18–Mar. 7. British Commonwealth Scientific Official Conference. Canberra and Melbourne, Australia.
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Feb. 25. Massachusetts Society for Research in Psychiatry. Cushing Hospital, Framingham.
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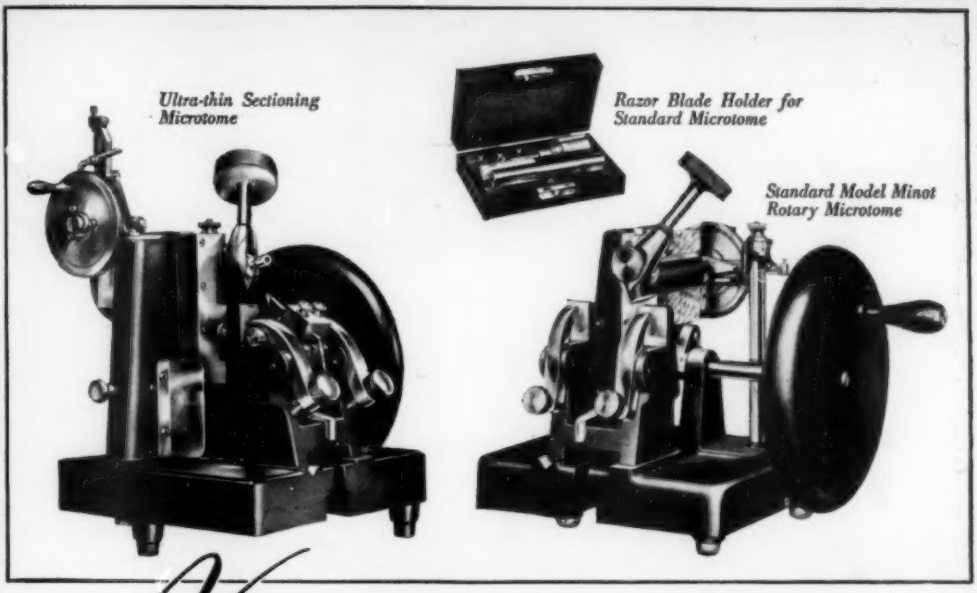

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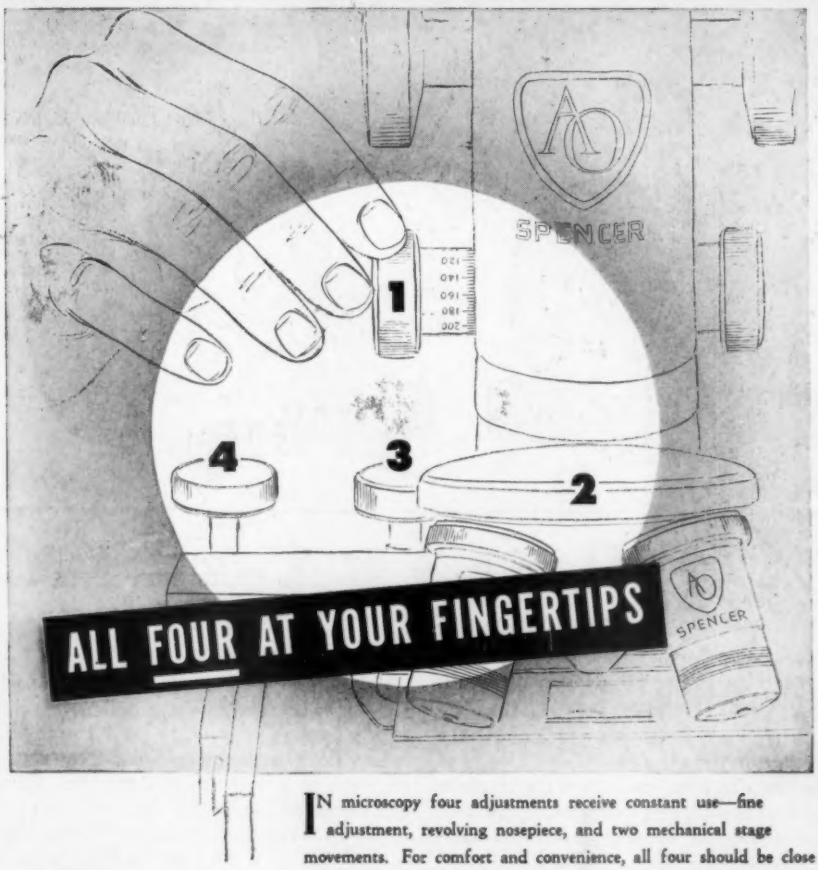

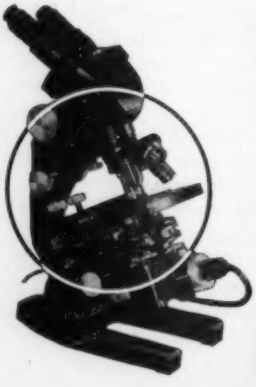

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